ARTERIOSCLEROSIS

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ARTERIOSCLEROSIS

A SUMMARY VIEW

BY THE LATE

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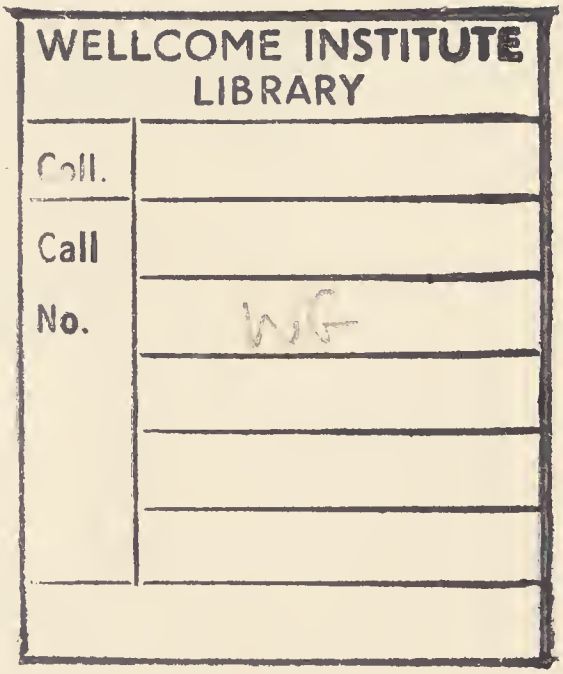

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PREFACE

This essay, now a little enlarged, was delivered as a Lecture to a Post-Graduate Class in Cambridge, and is now published in the hope that it may be found useful to the busy practitioner who has not time to consult my larger book, or the work of Dr. Batty Shaw;[1] still less to look up the many papers scattered through various Journals and Transactions. Perhaps indeed to those who have read the larger books a summary of the present state of our knowledge of the subject may be not unwelcome. Dr. Shaw's admirable work is founded upon a large practical experience, and is stiff with facts. In the first 74 pages forty-nine cases, closely watched and recorded, are analysed, classified, and compared with the pathological reports.

Since the publication of my larger work[2] I have collected many more cases, with necropsies, reinforcing and illustrating the distinction between hyperpiesia and chronic renal disease; but as such proofs now

[1] *Hyperpiesia and Hyperpiesis*, by H. Batty Shaw, M.D., F.R.C.P. London, 1922.

[2] *Diseases of the Arteries, including Angina Pectoris*, 2 vols., London, 1915.

abound, and this survey must be brief, I have given results only, postponing the case reports for some other opportunity. If I have had to change or amplify little of what I said in my work on Arterial Disease I have repeated some of it with various emphasis and under other conditions and proportions. It is to be hoped that the causes and the secret of the cure of hyperpiesia may be not very long hidden from us, for we are realising more and more the frequency of the malady; Dr. John Parkinson[1] speaks of it as "that very common disease which is responsible for so much suffering and mortality in late middle life and early old age".

For the convenience of the reader I have broken up my lecture into chapters.

CLIFFORD ALLBUTT.

[1] *Lancet*, 1924, ii. 481-5.

NOTE

During the last sixty years the late Regius Professor of Physic in the University of Cambridge made many additions to the science and art of medicine. Some of these are now so thoroughly incorporated in common knowledge and practice that our indebtedness in this respect is largely forgotten, such as the invention of the clinical thermometer now in use and the description of syphilitic disease of the cerebral arteries. His contributions covered a very wide field, but the cardio-vascular system received his special attention : for example, his stimulus to the study of blood pressure, his large share in establishing its routine use in medical examination, and his correct view of its relation to arterial disease ; his conception of hyperpies*ia* or high blood pressure of obscure origin as distinct from the raised blood pressure (hyperpies*is*) secondary to renal disease ; his advocacy of the aortic origin of angina pectoris ; and the influence of strain and overwork on the heart and arteries. These subjects he continuously elaborated in the light of his fresh observations and correlated with the work of others, on which he kept an ever-watchful eye, so that even since his great work on *Diseases of the Arteries, including Angina Pectoris* came out in 1915 his views have matured, and therefore should be eagerly read by his numerous friends, pupils, and admirers in the profession he so greatly adorned. Mentally as young and progressive as ever, he had lately been conscious of some physical failure, and indeed had decided to retire in July, when he would have entered his ninetieth year. He therefore felt anxious to finish this—his last utterance—and succeeded in completing a work which contains references to papers by others published so recently as January of this year ; but his sudden death, after ten minutes' acute distress, on 22 February, 1925, occurred before any proofs were available. It is a privilege to have been entrusted with the task, light as it was, of seeing through the press the last words of this great and beloved master.

HUMPHRY ROLLESTON.

April 1925.

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ARTERIOSCLEROSIS

CHAPTER I

Our Meanings

Gentlemen—It may seem to you that I have chosen rather a trite subject for my lecture to-day. The path is well trodden, it is true, but we may find reason to suspect that it is not yet all soundly laid, and not infrequently leads us to wander in a circle; moreover, around it is an unexplored or an unsurveyed wilderness. We may suppose that we know all about "arteriosclerosis"; but I fear, at any rate for myself to-day, that we may find ourselves with scanty stuff to put up much of a show. Indeed our path is somewhat cumbered with flimsy and alien materials; and when these are cast aside—and more than one bold man has proposed that we should begin by casting out the equivocal name of arteriosclerosis itself—the way before us may look rather bare.

Terms and Phrases.—We say that such a one "has got arteriosclerosis". What do we mean? From one aspect of diagnosis his arterial changes may be consistent with a life of fourscore years; from another he may be under the imminent menace of death. Some physicians give this name to cases in which,

though the arterial pressures run high, no arteriosclerosis has yet become apparent; but, as Cohn[1] says, "hyperpiesis is not a sub-heading under arteriosclerosis". So again recently we hear from an eminent professor of "the syndrom of arteriosclerosis", from another of the "symptoms of arteriosclerosis". What are they? We are apt to form certain fixed habits of speech and thought, habits which hinder or warp the free play of our minds; and we hamper ourselves with abstract phrases, or are content with phylacteries, such as "intestinal toxins", "compensation",[2] "morbid entity", and many another which need much sifting and at least some evidence. As Prof. Oertel of Montreal says, "Pathologists at large have not yet learned to distinguish between what is scientifically established and what is assumed". "Intestinal toxins" is one of the most pertinacious of these catchwords; as some one said of another matter, "We are guessing in the dark about a guess in the dark".

In an interesting article (*Lancet*, 1924, ii. 639), by Drs. J. Eason and G. Smith, an eminent cardiologist is quoted as saying, under the head of family proclivity to nephritis, "that this tendency appears with a like tendency to early arterial degeneration, early cerebral hæmorrhage, myocarditis, or angina pectoris . . ."; and again to contracted kidneys: "these maladies being distributed in a family, or piled upon one or more of its members". Indeed the authors themselves likewise hardly distinguish hyperpiesia,

[1] Nelson's *Loose-Leaf Living Medicine*, iv.

[2] Compensation is used far too much with a teleological meaning; it is better to be content with the law of reciprocal action.

primary contracted kidney, myocarditis, and the atrophic kidney of the so-called "senile" arteriosclerosis. Families probably do vary in the relative durability, viability, or age of maturity, of particular organs; some families in one direction, some in another. Certain nervous diseases especially suggest such inequalities; nevertheless the comprehensive view of these authors surely is too huddled, too general, general to the degree of vagueness and confusion. Primary contracted kidney is probably the issue of some long foregone infection, acting, it may be, on a naturally frailer kidney; hyperpiesia is probably due not to any renal disorder but to some wry metabolism pouring into the circulation a pressor body or bodies; the "arteriosclerotic kidney" is unattended by high pressures, and is not a nephritis at all, but is the slow atrophy of a kidney whose vessels as channels of nutrition are impaired (p. 57) (Lorrain Smith and Allbutt, and others); cerebral hæmorrhage is an accident due to disease of vessels from any cause—in syphilitic gumma, for example—with or without high pressure; the alleged "myocarditis" of hyperpiesis is a state of an overgrown, over-laboured, out-fought myocardium presenting no inflammatory elements, unless it be an exceedingly slow quasi-reparative fibrosis (p. 63). We are, then, too much given to abstract terms and speculations; we lack the concrete of our forefathers, the homely touch, forgetting that the fire painted on the wall did not warm the old woman. Caution with a suspended judgement is one thing; it is another thing to leave our notions unexamined and disorderly. Or again, like our neighbours

in France, we may be too categorical ; as Wepfer says, in his excellent book on apoplexy (1658), our reason invents systems which nature eludes. We shall have to turn over some of these stones to test some of these abstract terms ; we shall find that we know less than we thought we did.

If, then, we either discard the term arteriosclerosis or deliberately use it in a very general sense,[1] what preciser term or terms are we to substitute for it ? We have to-day to deal with diseases of the tunica intima and of the tunica media, processes that are far from identical ; indeed in itself neither is single. For the subintimal sclerosis the name diffuse hyperplastic sclerosis is in favour, but the adjective " diffuse " ignores its substantial identity with the same process when seen as patches in the larger vessels, such as the aorta. " Atherosclerosis " marks this identity, and seems to me a better name. " Hyperplastic " again seems a little too large an adjective for a very feeble reparative reaction. Disease of the media has not as yet received any distinctive name ; indeed there is more than one kind of it. " Hypertension " (or, to speak grammatically, hyper*tonus*—or *super*tension) denotes too narrow a meaning : " tension " can be predicated only of the proximal distended vessels, and in them it is not the essential factor ; the essential factor is the rise of blood pressure ; this the name

[1] The name might be narrowed to signify only that gradual fibrosis which from youth to age slowly invades all cardio-arterial structures, substituting itself for the " nobler " elements. But there is no likelihood that so restricted a meaning would be observed.

Hyperpiesis denotes, and it is coming now into general use. In hydrodynamics, moreover, the word "tension" is not used ; in fluids it is the pressure that is positive.

Another misleading term is "pulse-pressure" in the singular number. It is difficult to say how it arose. It is used to signify, not what it says—the pressure of the pulse—but the difference between the systolic and diastolic pressures ; the normal proportion being about 70 per cent. The intermediate curve is unknown. A far better term is at hand ; namely, the Differential Pressures ; a term intelligible to perplexed students and others. Or the term amplitude may be preferred. By rule of thumb, the differential pressure is normally about one-third of the diastolic, as the diastolic is about one-third again of the systolic. But, lying as it does between two variables, the differential pressure is unstable. Notwithstanding it should be recorded as some indication of the heart's load, and of its factor of safety or reserve. *Differential pressures* we understand at once as relative movements ; in the larger vessels, especially if dilated, wide and inconstant and, save for vasomotor tides, smaller and less variable towards the periphery ; *e.g.* in an artery of hand or foot ; as may readily be demonstrated with a Gaertner's sphygmometer. The fall in pressure from the brachial to a digital artery is about 20 mm.

As the larger vessels harden and dilate, systole is prolonged, and systolic pressure generally increases, while diastolic pressure falls towards zero. In aortic regurgitation the diastolic pressure may fall 70 or 80 mm. The larger arteries which should serve for

storage of energy, or as a flywheel between heart and periphery, as they harden approach the conditions of rigid tubing ; and the differential pressures so increase as to cause a jarring of the vessels, which can do them no good. So, as the arteries harden in age, the differential pressures tend to widen by loss of resilience and fall of the diastolic and some systolic rise ; if, then, the same stream volume is to be kept up, the heart must hypertrophy. (See p. 62.)

Once more ; in hyperpiesis, whether renal or not, the vessels are tightened with blood dammed back. The heart and main vessels are so full that the output of the ventricle against the resistance is less and less, while the distension of the arteries is pushed towards the outward limit of their elasticity ; thus their further function, as an elastic reservoir between heart and capillaries, of forwarding the blood during cardiac diastole is checked, and diastolic pressure rises.

If, then, arteriosclerosis be not a disease, but a feature of several diseases, *is hyperpiesia a disease* ? Dr. Batty Shaw has approved its title to this distinction ; and indeed I think its characters are now generally recognised. But what do we mean by a " disease " ? To say it is a " morbid entity " is to talk nonsense ; the entities are the patients. From a survey of certain patients having a general resemblance one to another we form a general idea, or concept, of a morbid series ; this concept exists nowhere outside our own brains ; and within them must vary somewhat from mind to mind. By a " disease ", then, we mean a concept of a series of symptoms, coincident and successive, positive and

negative, recurring in many and various persons with a fair uniformity. One of such series, or ideal patterns, is called hyperpiesia, a series lately distinguished from chronic Bright's disease. Usually it has a long and stealthy incipience ; often indeed, by filling the brain with blood, giving the patient for a while a sense of well-being and efficiency, but sooner or later revealing itself as an enduring and irresistible strain, racking even the strongest bodily system. As with cancer, too often these patients do not come under observation until the disease has fastened and extended itself upon the body.

Definition of Subject.—And, to come closer to our matter, I must on this occasion deliberately omit certain kinds of arterial disease ; for instance, syphilitic arteritis, arteritis obliterans, the arteritis of trauma, that of tuberculosis, and periarteritis nodosa. Another large omission has to be made, not because it lies outside my limits but because of our ignorance. One of our habits of thought is to think of the active circulation almost entirely in terms of the heart, arteries, and veins ; but we must remember that the blood is only one of the fluids circulating in the body ; the lymph and plasmatic fluids, with their solutes, also make up a copious sum ; the mere travel of these, and of the blood itself, is an accessory and mainly mechanical function compared with the complex biological and other reactions in the capillary, cellular, and circumambient fields ; such as the nutritive, cathartic, colloidal, osmotic, ionic, and intersurface actions. All these, and moreover the particular properties of the capillaries themselves, effective as

no doubt they are (p. 40), have their abode as yet in the unknown.

CHAPTER II

The Causes

Let us now consider the causes of arterial disease, or diseases ; and in the first place the *mechanical causes*. I will assume, on the strength of general agreement, that the rises of arterial pressure, with which we are concerned to-day, are due to vasoconstriction over large areas ; constriction of the minor arteries ; constriction, not " spasm " ; spasm seems an inappropriate term for a permanently heightened condition and attitude of tone and posture.

The history of the interpretation of cause and effect in arteriosclerosis is, broadly, on this wise :—v. Basch, studying arterial disease and blood pressure in Marienbad and Vienna, attributed such rising pressure to the resistance offered by thickened arteries. In the next place, Huchard, in Paris, reversing cause and effect, attributed the disease of the arteries to the damage done by the excessive pressures. Thirdly, it fell to the lot of the present writer to point out that in 50 per cent., or more, of cases of arteriosclerosis pressures were not, nor had been, excessive. The state of the heart has been taken as the chief witness to this factor in the past history. Meanwhile the studies on the structural pathology of the diseases of the vessels by Johnson, Gull and Sutton, Jores, Turnbull, Evans, Klotz, Andrewes, and many others, took a parallel course in time.

As regards the mechanical conditions, we may presume that the degrees of lateral and longitudinal stress upon the vessels must vary as the blood pressures and the internal friction pressures which may vary around the normal mean, or around some mean above or below. In this address I am concerned with abnormally high pressures only. I shall consider two of such disorders—especially the high pressures of certain renal diseases and those of the obscure and stealthy malady, said to be on the increase, to which I have given the now widely accepted name of *Hyperpiesia*—in these both the diastolic and systolic pressures may rise, the systolic to and beyond such degrees as 200 mm. Hg, and the diastolic to pressures of 160 and more. We may guess that such pressures, beyond the normal range, would tend to strain the continent vessels, to stretch them beyond their elastic limits. Again, if in any malady the blood pressures have not ranged above the normal mean, but the vessels have lost some of their quality, or were never of good quality, they might likewise suffer nevertheless. There are yield points in all structures, organic and inorganic, sound and unsound; beyond these their integrity is menaced, or actually sapped. Yet in the vascular consequences there is little apparent constancy. It is said that a high excess of blood pressure, maintained by cardiac hypertrophy, may be established—say, in certain renal diseases—in as short a period as four weeks; yet after a persistence of such high pressures for four, five, or even six years, during which the heart has been releasing energy rather in distension of the arteries than in propelling their content, the larger

vessels may still show no visible signs of injury. Whatever the contraction volume of the ventricle, the output per beat may be less than normal, perhaps much less ; and during these long periods of distension, as Sir James Barr has insisted, the vessels are held too taut to store up the energy delivered by the heart ; the circulation approaches that in rigid tubes, the vessels have no periods of rest, and the vasa vasorum of the aorta are squeezed dry. It is chiefly the high diastolic pressure, then, that aggravates the evil. The high systolic pressure of aortic regurgitation, though it batters the thoracic aorta, does not do all this widespread mischief. As Prof. MacWilliam remarked to me, cerebral hæmorrhage is relatively rare in aortic regurgitation ; but the mean age of the arteries is, of course, younger.

The vessels, then, and the heart, as one machine, suffer alike ; for at all costs the mid-brain circulation must be maintained (p. 50). Indeed that heart and vessel keep fairly sound for periods so long is a marvellous instance of our large factors of physiological safety ; but, wide as the elastic limits of their material may be, resilience has its limits. For the detection of invisible impairments of elasticity the method of Bramwell and A. V. Hill for recording the time of the wave velocity may become clinically available. However, if in a case of prolonged high pressures the arch of the aorta still shows on the face of it no patch of injury, yet if the parts be brought carefully together some dilatation will often be perceptible. Besides, for some obscure reason, atheromatous patches are often to be found, even abundantly, in the abdominal aorta when

the thoracic portion seems uninjured. This greater liability Professor Muir attributes to the hydrostatic pressure of the longer column of blood. A like thickening, by disturbance of linear motion, may be seen also at the offspring of branches, especially of those at sharper angles as at the intercostal. Probably also the finer vessels if unconstricted are more liable to damage under high pressure than the larger. In old age, under conditions of long duration, or of arterial tubes of lower quality (Osler), or of some coincident poison, we may see extensive atherosclerosis in vessels both large and small, even although blood pressures may not have been excessive.

That, however tenaciously resisted, mere high internal pressure and friction may suffice to damage and break up the vessels is illustrated by the many instances of this effect upon the pulmonary artery and its branches in cases of abnormal resistance in the pulmonary area ; for example, in long-standing mitral stenosis with hypertrophy of the right ventricle.

These cases of purely mechanical atherosclerosis may be distinguished from those in which the vessels decay under the influence of toxins such as those of enteric fever, influenza, or even pneumonia.[1] In these toxic cases, in which the right ventricle may not be hypertrophied, the damage usually begins in the media and extends to the smallest ramifications ; mechanical strain on the other hand sets up the atheroma (atherosclerosis) of the subintimal tissues. The illustration from the pulmonary side is instructive, seeing that

[1] Wiesel und Löwy, *Wien. klin. Wchnschr.*, 1921, xxxiv. 289 (see p. 27).

it discriminates for us these diverse modes of the systemic side.

On the mechanical tests of arterial resistance in animals, as by suspension, by adrenin, and so on, I will say only that they are too acute, too severe, for comparison; they are blows rather than gradual strains; so acute that there are no perceptible attempts at repair. Necrosis of the media seems to be the outstanding result of such experiments. Marabotto,[1] while experimenting on rabbits with adrenin, and thereby producing hyperpiesis and " arteriosclerosis ", found evidence of an " anti-adrenal body " in rabbits' serum. When he injected this body with the adrenin little change was produced; and he suggested that this anti-adrenal serum might serve normally to counteract hyperpiesis and its consequences. But if it has a lytic effect upon adrenal tissue its random use as a drug might be perilous. However, after all, as a petulant pathologist remarked the other day, " the hutch rabbit is a rotten little beast ".[2] The sequence of arteriosclerosis observed after injections of cholesterol is open to the same criticism. All atherosclerosis, whatsoever its causes, contains cholesterol.

In proceeding to consider *pathological causes* of

[1] Marabotto, *Ann. dell' Instito Maragliano*, 1916, V. viii.

[2] A remarkable instance in point is given by MacCartney in the *Studies from the Rockefeller Institute*, 1924, xlix. 87. A long series of experiments on epidemic encephalitis was vitiated by the discovery that in the large stock of rabbits in the laboratory, many of which were untouched by experiment, others by no kindred experiment, and all apparently in good health, were found to present infiltration of mononuclear cells in the meninges and vessels of the cortex, due to a bacterial infection to which the hutch rabbit is prone.

arterial damage we do not then set aside the mechanical. With or without excessive pressures wear and tear must, of course, be reckoned with in all cases.

A current notion that the mass of blood in the body may affect the blood pressures we may dismiss at once ; only very rarely, incidentally, and partially could this happen with any bulks of blood mass we are likely to have to consider. The work of the heart it will affect, but not the arterial pressures. There are ample reservoirs — splanchnic and other — to accommodate such volumes, and the readjustments by the nervous system are rapid. The repletions artificially obtained by injection of fluid into animals have no counterpart in clinical medicine.

Of the pathological causes we will begin with *the renal* ; of these we know a little, of the rest we know less. We suspect that in all diseases of the kidney there is a chance of a rise of arterial pressures ; but in the majority, perhaps the large majority, of cases of chronic parenchymatous nephritis without much destructive glomerular disease, arterial pressures are unaffected in this way ; on the other hand pressures rise in every case of primary contracted kidney, and in most cases of secondary contraction wherein the glomeruli are widely affected. The " senile " or " arteriosclerotic " kidney (the " atrophic kidney "), even if advanced, causes no excess of blood pressure (see p. 57).[1] In acute glomerular nephritis on the other hand, *e.g.* in scarlet fever, pressures rise rapidly ; sometimes even before albumen or blood appears

[1] Lorrain Smith and Allbutt ; H. Maclean (*Brit. Med. Journ.*, 1922, ii. 1067) ; and others.

in the urine, or latent œdema raises the weight of the body.[1] It seems then (*pace* Jores) as if the Malpighian system were chiefly concerned in this event; whether by fibrotic strangulation or disease of the tufts. Mere atrophy of the tufts, as by sclerosis of renal vessels, unless very extensive and far gone, does not lead to high pressures. One of the simplest cases of renal causation is that, narrated by Dr. Batty Shaw, of compression of the kidney by a hydronephrosis;[2] the arterial pressures rose until this kidney was removed by operation, when the pressures soon dropped to the normal. Bryant and Hale-White[3] published a like case; and Dr. G. Evans[4] thinks that the cause as regards the kidney lies not in its positive but in its negative function; in non-elimination. I have said that the renal area is far too small to affect the general arterial pressure by its mere closure; Esmarch's bandaging of both legs sends up the pressure only some 15 mm., and this transiently. But there is some evidence, not yet conclusive, that from the quite fresh kidney, removed instantly on death, a pressor substance can be obtained which has been named "renin" (Tigersted, 1898; Vincent and Sheen;[5] Batty Shaw and Schryver[6]), which acts directly upon

[1] Monakow, Kylin, Lindberg. See also Kylin, *Zentralbl. f. inn. Med.*, 1921, xliii. 441.

[2] Shaw, Batty, *Hyperpiesia and Hyperpiesis*, p. 166 (chart 52), 1922.

[3] Bryant, J. H., and White, W. H., *Guy's Hosp. Rep.*, 1901, lv. 17.

[4] Evans, G., *Quart. Journ. Med.*, Oxford, 1922–23, xvi. 33.

[5] Vincent, S., and Sheen, *Journ. Physiol.*, London, 1903, xxix. 242. Professor Vincent regards the hypothesis of a renal pressor substance in contracted kidney as unproved.

[6] Shaw, H. Batty, *Lancet*, 1906, i. 1295.

the muscular arteries, independently of the nervous system. That the renal arterioles suffer first suggests that the sclerosis is not due, or not due only, to mechanical strain.

The hypothesis that renal hyperpiesis is secondary to an irritation propagated from morbid kidneys to the adjacent *adrenals*, save perhaps as an occasional coincidence, is abandoned.[1] The effect of adrenin thus produced would in any case be transitory.

A contrary hypothesis, that all cases of hyperpiesis are essentially, if often latently, of renal origin is now likewise abandoned. Experienced observers, both clinical and pathological, are generally agreed that persistent and extremely high arterial pressures, as for example in the morbid series or syndrom now known as hyperpiesia, may prevail and this to mortal issues, notwithstanding intact kidneys and normal nitrogenous urine and blood concentrations.[2] Ligation of both renal arteries does not of itself raise the arterial pressure; and it is said that the serum of these hyperpietics produces no abnormal pressor effect upon a normal circulation. We can hardly assert, then, that excessive rises of pressure are always due to failure of renal catharsis; in many cases they seem to be due rather to some swerve of metabolism. Jaffé,[3] who finds the afferent arteries of the kidney distended under hyperpiesis, thinks that a sclerosis thus produced, by starving the kidney, leads to chronic

[1] Elliott, T. R., *Journ. Physiol.*, London, 1914, xliv. 374, and many others.

[2] Batty Shaw, *loc. cit.*; Williams, J. L., *Arch. Int. Med.*, 1921, xxvii. 748; xxviii. 426; the present writer, and others.

[3] Jaffé, *Am. Journ. Med. Sci.*, 1925, clxix. 88.

interstitial nephritis. But the hypothesis that " granular kidney " owes its origin, as often in young persons, to some foregone latent infection, has far more evidence in its favour. (See also Senile Kidney, p. 57.) Klein [1] is disposed to regard all hyperpiesis as chronic renal disease or preliminary to it; but long experience of hyperpiesia is against this opinion. Sufferers from hyperpiesia are, it is true, liable to intercurrent renal disorder, but in later stages and of the catarrhal not glomerular kind.

The rises of pressure incident to large artificial saline injections into a vein, or occasionally to defect of aqueous discharge, are transitory, self-healing, and from our point of view negligible [2] (p. 13). The same may be said of degrees of viscosity of the blood. Thus, whether we seek on the one hand to explain the high pressures, or on the other the origin of atherosclerosis, whether under high pressure or not, we are still much in the dark.

In necropsies, I repeat, the best witness of long persistent high arterial pressures during life is the heart, by its relative weight; for atherosclerosis of the smaller arteries among the viscera due to hyperpiesis may be widespread (Jores) before changes in the large arteries or even in the brachial and radial become conspicuous; though in such cases *the heart* is always increased. It is hypertrophied and dilated, especially in its left ventricle; and, if the coronary circulation

[1] Klein, O. D., *Deutsches Arch. f. klin. Med.*, 1924, cxliv. 207.

[2] See Miller and Williams, *Trans. Assoc. Amer. Phys.*, 1920, xxxv. 75, and others. We used to prove this again and again in Roy's laboratory.

be impaired, more or less diffuse fibrosis may be seen around the myocardial bundles. The fibrosis seems to be just the atrophic result of fatigue, not necessarily of toxic origin ; although it seems probable that the primary contracted kidney is itself a long protracted result of an infection, such as of scarlet fever, diphtheria, streptococcal or pneumococcal sepsis, and so forth, creeping forward in latency for years after an apparent recovery from the acute attack. Cellular infiltration invades the Bowman's capsules, the glomeruli become hyaline, fibroid, necrosed ; and the cortex retracts (Councilman, Klotz, and others). The concomitant disease of the larger arteries of the renal system may be due to the hyperpiesis, and theoretically be not an essential factor in the nephritis ; though more probably it is initiated by the original infection.

To this audience it is not necessary to dwell upon the significance of high blood pressures in the pregnant or *parturient woman*. In the last pre-natal month and in childbed, even if no ill symptoms appear or be felt, it is right to record the blood pressures occasionally. " Forewarned is forearmed " is a venerable proverb.

Concerning *dietic causes* we have been rather too confident. We have assumed, on the old tradition of plethora, that high blood pressures are due, at any rate in many cases, to overfeeding, positive or relative, and especially on animal foods. The therapeutic effect of revisions of diet is, however, very disappointing ; and experimental results in this way are, to say the best of them, equivocal. As I have supposed, the secret probably lies in the metabolic perversion ; to speak metaphorically, a slip in delivery of protein

elements into an alternative space of a " lattice " ; or perhaps a reversion to a more rudimentary metabolic scheme (p. 23) ; or, again, the loss of a catalyst. There may be but a knife-edge between the slides of function one way and another.[1] That the hereditary factor is considerable I have no doubt ; most of us have witnessed its transmission both in frequency and severity in many a family ; perhaps a transmitted tendency to shunt metabolic processes on to an eccentric route, to the formation of pressor substances, such as tyramine iso-amylomine (Bain), or guanidine.[2] Calcium and the parathyroids are suspected of some part in the conspiracy.

Probably the blood pressures are balanced by the centres of the mesencephalon, as is the temperature ; the dorsal vagus nucleus being affected indirectly from this same area. There may be still higher regulative control : *e.g.* corpus striatum—to mesencephalon, to sympathetic, and para-sympathetic.

Obesity.—We may be the more prone to refer high pressures to high feedings because of a certain liability of fat people to hyperpiesis. Many hyperpietics are not fat ; many indeed are of spare habit and abstemious life ; but the percentage of hyperpiesia in the obese seems to be relatively high. At the menopause most women fatten, and therewith, in not

[1] See the well-known papers by Sir A. E. Garrod, *Inborn Errors of Metabolism*, 1923, and by other authors.

[2] Major and Stephenson, *Johns Hopkins Hosp. Bull.*, 1924, xxxv. 140, 186. Major, *Journ. Amer. Med. Assoc.*, 1924, lxxxiii. 81. (In a letter to me Prof. MacWilliam remarked that if guanidine raises blood pressure, the rise should be seen in tetany —parathyroid defect.)

a few, the arterial pressures rise somewhat. Probably in the majority of these cases the rise, which is said to precede the cessation, is transient ; or it abides at a moderate, and perhaps harmless, standard, such as 150-160 ; and the pulse, even if the arteries be a little stretched, keeps fairly soft ; but in others higher records, with thoracic oppression, growing heart, and other symptoms, persist. Faber,[1] in nine women suffering from "hypertension", found that the mean bodily weight ranged above standard by 16 kilos. Sir H. Rolleston [2] and Dr. John Parkinson agree in this experience ; as does also Dr. Symonds in a recent Report of the Mutual Life Assurance of New York. Dr. Parkinson says that symptoms in such subjects are often wrongly imputed to other causes.[3] Dr. Ackerley, who has treated three of my fat patients very successfully at Llandrindod, has long been convinced that there is a connexion between obesity and high pressures ; but he discriminates between the obese who thus suffer and the obese who do not ; saying that these stout persons tend to hyperpiesis, even of high degree, whose fat is hard ; while the flabby obese escape this consequence. He suspects that the hard fat acts in some way mechanically. Certainly in two "hard fat" patients of mine the cure, or relief, by careful reduction of bulk has been remarkable and, moreover, abiding. Pavlov has

[1] Faber, A., *Ugeskr. f. Laeger*, Feb. 21, 1924, p. 151 (quoted Epit., *Brit. Med. Journ.*, 1924, i. No. 474).

[2] Rolleston, H., *Newcastle-upon-Tyne and North Count. Med. Journ.*, 1923, iii. 71 : he quotes Aubertin and Coursier, *Presse méd.*, Paris, 1922, xxx. 72, to this effect.

[3] Parkinson, J., *Lancet*, 1924, ii. 481.

proved that the mere eating of a meal does not raise the blood pressures. It has been said of late that in the obese it is an arteriosclerosis which causes the rise of blood pressure. I need not stay to contradict this proposition.

Concerning *alcohol*; it seems now to be generally agreed that mere alcohol is as such no cause of hyperpiesis [1]; yet I would still reserve the subordinate question whether when it forms a part of a rich diet it may have a co-operative, if subsidiary, influence. Furthermore, I find no later evidence to weaken my opinion that the effect of tobacco in causing hyperpiesis or senile atheroma, if any, is negligible.

That *gout*, in its uncomplicated arthritic form, is no cause of hyperpiesis is still my opinion; although the systolic pressure may well rise during the pain of an acute seizure.[2] Indeed arthritic gout seems to be an alternative issue—the one or the other, not both. Yet, notwithstanding, I think still that there is some affinity; that hyperpietics often report gout as "in the family"; or the patient himself at some earlier date may have suffered from gout. I am told, moreover, by biochemists that the normal excretion of pressor substance in the urine is not held up in gout. The maladies may be kindred, though several, disorders of metabolism variously inherited.

[1] See *e.g.* Kent, S., *Lancet*, 1917, ii. 107; and my book on *Diseases of the Arteries*, 1915, ii. 246.

[2] See also E. N. Rosenbloom, *Journ. Amer. Med. Assoc.*, 1918, lxx. 26. (Four cases of podagra tested over long periods of time.) I may add the case of an old gentleman, who had his last and worst attack, in both feet, when he was well over the age of 80. He died two or three years later of senile decay. There were no phases of high arterial pressure.

Again, in my work on Arterial Disease I stated that arteriosclerosis of the low pressure kind was frequent in *diabetes*, and ran in children. This statement has been questioned, on the ground no doubt of some exceptions. However, this is the rule ; I repeat that even children often present this association of signs. To test the rule again, a few days ago, in passing through the wards of our hospital, two or three of us examined the accessible vessels of three diabetics. The first case, in a girl æt. 14, was inconclusive ; we doubted whether or no the radial were a trifle too palpable for her age ; although in diabetes I have found well-thickened arteries, male or female, at ages younger than this. The second patient was a young man æt. 24 ; a severe case of apparently sudden onset three months before ; his previous health had been good. His radials were tape-like, and brachials tortuous. The blood pressures were, if anything, under normal. No history nor sign of syphilis. The third patient, a fine young man æt. 32, presented the same features, both positive and negative. The anatomy of this thickening in diabetes I do not know ; I have never been able to secure a strip of such an artery from a necropsy. It seems improbable that in young subjects the diabetes should be an effect of a foregoing atherosclerotic atrophy of the pancreatic islands ; the vascular thickening is probably an unexplained effect—ionic or other—of the disease itself. The blood pressures in diabetes are inconstant and depend upon incidental factors.

It has been confidently asserted (Marchand, Allbutt, and others) that arteriosclerosis may be set up in

limbs by prolonged *muscular exertion*, even in comparatively young persons; as, for example, in the labourer's arms, or the postman's legs; if so, care must be taken not to infer from the limb a general arterial disease. The sclerosis is medial; a fatty degeneration of fibre, then soaps and calcification (Klotz, MacCallum). My own opinion was founded some years ago, while serving on a Home Office Committee, on an examination of a large number of presumably healthy labourers shepherded up at hazard in certain large "works". However, this opinion is called in question by Fisk,[1] whose experience in examinations for Life Assurance is very large. In this respect he compared large numbers of labourers with an equal number of bank clerks and the like, and found the conditions of the limb arteries to be about the same in both classes. Hospital practice, however, seems to me to show that in labourers at and under middle age arteriosclerosis in the limbs is more than ordinarily frequent; it is true that often their conditions of life may be faulty in many ways.

Infections.—The stereotyped notion of the causes of arteriosclerosis is *toxic*, a vague adjective which means little; "*intestinal toxins*" is one of our transferable tickets, or phylacteries. Professor Adami also has protested against the abuse of this formula. That some poison or other is at work in the production

[1] Fisk, E. L., *New York Med. Journ.*, 1916, ciii. 97. We are receiving very valuable information from physicians to the American Insurance Companies, also from Drs. Fisk, R. L. Mackenzie, Faber, Fisher, Symonds, and others.

of some kinds or degrees of arterial deterioration is probable ; but in cases of hyperpiesia time after time I have failed to elicit any evidence, though diligently sought for, or even any suspicion, of disordered intestinal functions. As Alvarez points out, the well-known discomfort and biliousness of constipation are removed so instantly by a purge that they cannot be due to a poison circulatory in the blood. And they can be artificially set up by plugging the rectum with cotton-wool. The urine is, as a rule, free from indican, and injections of indol do not affect the blood pressures. We need proofs, not bare assertions. Intestinal poisons are indeed, generally speaking, of the depressor class ; and cases which in practice one suspects may be of intestinal origin are not in ruddy and active, but in sallow, torpid, and clammy persons. Now the majority of hyperpietics during the first years of increasing pressures enjoy excellent health ; I say "excellent" and "enjoy" because many of them for a while are energetic, well complexioned persons with brains fully supplied with blood. If the amino-acids, which can and do pass through the vigilant intestinal mucous membrane, after passing the custom house of the liver, are in excess of the body's needs, they are got rid of, probably harmlessly, as ammonia and CO_2 (Folin ; Hopkins). I reiterate that in hyperpiesia I suspect the cause to be a warp of metabolism, possibly in the liver ; an incomplete or skew reduction of noxious waste turning out some pressor amine, or hampering its exit, or failing to convert it.

However, the high pressure arterial disease is far

from covering our field ; we have to account for that large, indeed larger, class of arteriosclerotics in whom I showed that arterial pressures were and had been normal, or virtually normal. Physical *wear and tear* plays some part ; the vessel suffers a shearing strain at its weakest part, namely, along the apposed surfaces of intima and media. Adrenin seems not to be the disturber ; its pressor effect is transient, its glands are not found to be altered in these cases, a heavy output soon exhausts them, and experiment has shown that in hyperpiesia there is no excess of adrenin in the blood. It seems to me that, in laboratory animals at any rate, the secretion acts more as a poison than by mere mechanical stress.

Yet we know that there are poisons which affect the vessels ; *lead* is one of them : but this effect may still be by strain, as, with " granular kidney ", lead causes wide vaso-constriction, and injures both intima and media. Indeed Sir W. Willcox has said that for every variety of arterial disorder which Dr. Batty Shaw might describe in man or animal the toxicologist, by some drug, could furnish its counterfeit. Sir Humphry Rolleston, in an interesting essay,[1] agrees with Dr. Batty Shaw in accusing *excessive protein food*, as thereby the endocrine balances are disturbed ; but with this fault Rolleston associates worry, adverse circumstances, disordered metabolism, and intestinal toxins. This is to spread the net rather widely.

Dale and Dixon [2] and others (Abelous, Bain,

[1] Rolleston, H., *loc. cit.*

[2] Dale and Dixon, *Journ. Physiol.*, London, 1909–10 ; and Barger and Walpole, *ibid.*, 1909, xxxviii. 343.

Barger, Dixon, and Inchley) take a different, or at any rate a more definite, view of the problem; they have found pressor substances in *extracts and putridities of meat*; and suppose that these, by some kakobolism or parabolism, find their way into the circulation. Normally these substances are converted into the ammonia so abundant in the portal vein (Folin). It is well known that in the higher divisions of the intestine chemical poisons of increasing virulence are generated; in man they are best known to us in injured bowel, as in high obstructions; but these should not be absorbed through a normal endothelium, or in any case should they be neutralised by a healthy liver: moreover, these poisons are for the most part depressor, or asphyxiating, rather than irritative or pressor. It is agreed that such poisons "are relatively simple bodies, no more complex than the alkaloids".[1] Instead of being broken up into ammonia, CO_2, etc., they may be earlier perversions of amino-acids by means of putrefactive microbes. The normal liver is the chief warden of these marches, and now by many observers *pressor amino-bases* have been demonstrated as escaping in the urine. They are said to be absent from the urine in childhood, to appear about the age of fourteen, and normally should persist throughout mid-life and old age. Dr. Bain[2] says that in hyperpiesis these bases disappear from the urine, though, as Dr. Dixon remarks, they may be more completely destroyed, in the liver or otherwise; especially in experimental feeding by the mouth. A diet of eggs, vegetables,

[1] Dixon, W. E., *Lancet*, 1913, i. 1295.
[2] Bain, W., *Lancet*, 1911, i. 1409, and later papers.

and fish reduces them in the urine. It is said that by experiment with bases such as these arterial pressures have been raised, and that by certain variations of diet they may be made to come and go ; but in these comparatively few researches we are as yet far from certainty ; further series of experiments and tests are to be desired, and offer some promise of light.

Loeb [1] produced atheroma of the aorta in five days in rabbits by injections of lactate of sodium, and found that a previous injection of egg albumin prevented this effect. Although this statement has been verified by others (Mönckeberg, Bender, and Klemperer), yet, as I have said (p. 12), these acute experiments upon hutch rabbits cannot carry great weight. The same may be said of the causations of atheroma in these animals by injections of cholesterol. Neither can we assume that we have arrived at such simplification that we can refer all these maladies to such vast abstractions as hydrations and dehydrations ; to acidæmia and alkalæmia—dividing mankind into the tribes of anionites and cationites,[2] nor again to vagotonia and sympathicotonia. As suggestions they are interesting and nourish the scientific imagination, but they lie as yet in the mists of conjecture. Acids, by action on the kidneys, may tend to raise blood pressure ; but unless the acid be excessive the ions are merged in the stream of physiological compensations and contingencies.

The mischief which may be done to the arteries

[1] Loeb, *Ges. Med. int. u. Pediat.*, Berlin, July 6, 1914—quoted *Arch. mal. du cœur*, Dec. 1915.

[2] McClure and Ellis, *Lancet*, 1921, ii. 271.

by certain of *the infectious diseases* was set forth by Wiesel nearly twenty years ago.[1] In his paper Wiesel goes through these diseases with a fullness beyond my brief reporting, and shows how media and elastica may be permanently damaged by them. The intima suffers less, and secondarily. The damage is patchy and may heal by scar; it is seen best in the aorta and in the cardiac and the cerebral arteries. Some of the cases of juvenile arteriosclerosis find thus a probable explanation.

Of scarlet fever we know that a consequent rise of pressure is generally secondary to a nephritis; the same is true of trench nephritis, in so far as it was followed by rise of arterial pressures; but this effect was seen in the minority of cases (25 to 33 per cent.).

In influenza, so severe as to lead to necropsy, Störk and Epstein[2] found the arteries gravely affected; they report necrosis of the muscular coat in patches, and fragmentation of the elastica. Aortitis after influenza, no very rare event, I have described in my Arteries book. The coronaries also are liable to suffer in like sequence; the cerebral vessels and the pulmonary (unless pneumonia be present) for the most part escape.

Typhoid and paratyphoid fevers may give rise to visceral arteritis—or arteriolitis—(Rolleston,[3] Rendu, Barié); sometimes to a mild "parietal arteritis".

[1] Wiesel, *Wien. Ztschr. f. Heilk.*, Wien u. Leipz., 1906, xxvii. 262; subject also well discussed by Batty Shaw (*loc. cit.*).

[2] Störk, S., und Epstein, E., *Wien. klin. Wchnschr.*, 1919, xxxii. 1086.

[3] Rolleston, J. D., Translation of Vincent and Muratet's *Fièvres typhoïdes et paratyphoïdes*, 1917, p. 44.

When for some years I had full charge of the Leeds Fever Hospital I often observed that the accessible arteries of typhoid convalescents had thickened; though I cannot appeal to any post-mortem records. Again, as J. D. Rolleston says, thrombosis of the posterior tibial artery (and I may add even of the femoral) is among the graver mishaps of typhoid fever.

To syphilis in this summary I hardly venture to allude; it would occupy a lecture to itself. Dr. Turnbull[1] thinks syphilis does not produce *general* arteriosclerosis; that cardio-vascular changes of this diffuse kind in the syphilitic show no more than the mean incidence. If so, I must suppose that I have lighted upon a large proportion of exceptions in persons not beyond middle age. It is true that many patients with a long syphilitic history and obvious signs still have their accessible arteries unthickened; but my experience has been that in not a few of them this change does come about. Some tiresome critics assert that such arterial damage is done by the doctor, by our use, or abuse, in syphilis of metallic drugs; if so, our therapeutical path will be a thorny one. But of syphilitic aortitis, and of syphilitic disease of the cerebral arteries, I must not repeat what I have written in my *Diseases of the Arteries*.

It is worth mention that Dr. Elliott of Chicago,[2] in 43 cases of chronic interstitial nephritis with high pressures and thick vessels, a list from which every

[1] Turnbull, H. M., *Quart. Journ. Med.*, Oxford, 1914–15, viii. 201.

[2] Elliott, A. R., *Journ. Amer. Med. Assoc.*, 1917, lviii. 1956; and see several papers by Moschowitz, E., *e.g.* that read May 16, 1922, Sect. Int. Med. Acad. Med. N.Y.

possible composite case was excluded, tested each one for the Wassermann reaction, and one only was positive. I may add that syphilitic nephritis, in its earlier and acuter phases, does not raise the arterial pressures ; though this may be the ultimate issue, as with fibrotic kidneys of other causation in which large numbers of the glomeruli become involved.

It is hardly needful to add that the possibility of consecutive arterial affection is one argument the more for diligent search for, and eradication of, *septic foci* of any kind in the body, apparent or occult.

As concerns the paths and occasions of arterial tissue infection we know little. We are ready to say that it enters by the vasa vasorum. Erasistratus of Alexandria, more than two thousand years ago, said that the arteries are nourished by vessels in their walls, which, of the aorta and larger vessels, is true ; but Sir F. Andrewes, and Dr. G. Evans also, opined that the arterial system beyond the aorta must be regarded as extra-vascular, *i.e.* as regards the blood ; but what about the perivascular lymphatic fluids ?

In this superficial survey of the infective causes of arterial affections I have not attempted to distribute the kinds of causes to the kinds of arterial disease, whether, for instance, to media or intima. This would be an intricate and at present inconclusive study. Suffice it to say that for the most part these arterial changes do not raise the arterial pressures. So, again, "old age" covers many causes ; besides wear and tear, infections old and new, vessels originally frail, or deciduous ; and so on.

Of disarray in *the endocrine system*, other than

adrenal, as causative of hyperpiesis I can speak only allusively ; we possess as yet very little knowledge on the subject. Between the bitter tonic of Professor Swale Vincent's scepticism and the ardour of the endocrinophiles there are many opinions ; but few of them are as yet built upon solid foundations of facts. My impression is that the secret we are trying to discover does not lie in this domain.

The provisional conclusion seems to be that wear and tear, normal or abnormal, acting upon vessels of various original quality, is largely concerned in the production of atherosclerosis, yet notwithstanding, even in hyperpiesia and senile atherosclerosis there is reason to suspect a frequent co-operation of causes of an infective kind ; and in certain maladies an infective cause is sole or predominant.

CHAPTER III

Morbid Anatomy

Under this head I will briefly review such facts as we have learned in the morbid anatomy of the blood-vessels, so as to secure some foundation for more speculative opinions. Let me repeat what I urged some years ago [1]—that each organ has its own character of reaction to irritations or injuries. The reactions of the component tissues have their several ways until they find themselves in combination ; then the result in each group or organ is a blend of the potentials peculiar to each constituent. Thus in the

[1] *Diseases of the Arteries, including Angina Pectoris*, 1915.

kidney, compacted of sundry tissues, however various the morbid agents in kind, its modes of response have similar and consistent characters of their own; as likewise atherosclerosis, whether of pressor or non-pressor origin, is substantially the same. Not only so, but each organ has its specific susceptibilities to alien substances; one organ will suffer under a toxic invasion, or alien ingredient, which to others seems innocuous. And in smaller measure the same is true as amongst the parts of an organ; thus the renal and splenic arteries are far more liable to disease than those, let us say, of the mesenteric and intestinal,[1] of the hepatic, or of the voluntary muscular area; and so on.

Disregarding these affections, such as the syphilitic, which I am to omit, we know now pretty well the pathological features we are to discuss; the disease of the tunica intima, and the disease of the media, known indefinitely and confusedly as "arteriosclerosis". These diseases arise in some independence, though often concurrently. Of our knowledge of them Virchow laid the foundation; but I think George Johnson was the first to demonstrate decisively the apparent "hypertrophy" of the muscular coat of the *tunica media* which, as cause or consequence, pertains to conditions of high arterial pressure, as in primary contracted kidney. Strangely enough, this alleged hypertrophy, although widely admitted, has of late

[1] It has been supposed that sclerosis in the mesenteric area was so early and so extensive as to be the cause of a high general blood pressure. This is now known to have been an error of observation; the mesenteric arteries are not among those first attacked.

been somewhat neglected or ignored; perhaps because it belongs to the earlier stages of disease when necropsies are few; and in later stages is merged in fibrotic or amorphous degeneration. Moreover, in Johnson's time attention was drawn away from this to another more general change, described by Gull and Sutton under the title of "arterio-capillary fibrosis". Johnson and Gull and Sutton were friends of mine, and I saw and compared their fresh preparations. A medial muscular thickening in Johnson's cases was beyond question; but, relying upon it and assuming it to be universal and precisely a hypertrophy, as contrasted with contraction or fibrosis, he was a little blind perhaps to other morbid changes in the vessels, and to the results of other pathologists. Moreover, Gull and Sutton's preparations were deceptive, because of the imperfection of contemporary methods of preparation; so that now we rely upon later records, yet without forgetting the great services that, in their day, these pioneers rendered to arterial pathology.

In cases of high arterial pressures, whether it be a true muscular hypertrophy or not, at any rate a *thickening of the media* is obvious, as, for instance, in cases of primary contracted kidney; and, as Dr. William Russell reminds us, this thickening alone may give to the finger at the wrist the sense of a sclerosed vessel; this may be felt even in young subjects, though in them the thickening may subside. Therefore the question of its nature is one of practical importance. One good and ready test of its nature is to place the whole forearm in warm water, when in about three minutes the radial may expand.

For my own part I have never felt assured about the hypertrophic nature of this thickened muscular coat. Why should the coat hypertrophy? How do we distinguish, microscopically or otherwise, between a thickening of the coat and of its several fibres, between a contraction and a hypertrophy; *i.e.* a numerical increase of the fibres, or an enlargement of each muscular cell in all dimensions? What standard have we to guide us? Certainly not the inconstant lumen of the vessel. Again, why should one position of tone call out or use more energy than another? An eminent physicist whom I consulted on the matter thought that the work done, little enough anyhow, would prove to be internal only, a release of energy during the act of contraction or dilatation, the passing from one attitude to another; and this would be almost incalculably small. My own impression is that the state is one of increased tone only, under the influence of some ergot-like poison. But, it is replied, there is more than an increase of tone; under such a poison the morbid increase of arterial pressures is general, systolic and diastolic; a "high tension". But in the peripheral areas with which in particular we are now dealing, by this very constriction the internal pressures must surely be lowered, the vessels being partly emptied. It is true that by the reaction of cardiac hypertrophy the pressure head is increased, but even then within the constricted areas it can hardly rise to the normal, and surely cannot exceed it. Constriction, then, must protect the vessels against strain, unless the passing blood be poisoned. The peripheral belt of constriction may be narrow or

wide ; it may, for instance, be confined to vessels on the farther side of arteries of the order of the radial, or may include these, or even vessels larger still ; then the tensile stress would fall on the walls of the vessels central to the belt, vessels unprotected by constriction ; especially on the elastic vessels. Professor Robert Muir, whose kind help I gratefully acknowledge, regards the hypertrophy of the media—" a real increase of tissue "—as not only apparent but actual ; and says that in the earlier stages it consists mainly of muscle and elastic tissue ; he finds it throughout the arterial tree, from the aorta outwards. In later stages it undergoes fibrotic degeneration. He agrees that the lumen of the vessel under observation cannot be taken as a standard ; so with the altered vessel he compares one of the same magnitude—say the radial in both cases—taken from a relatively normal subject. This hypertrophy he attributes to reaction against internal pressure, which is true enough for vessels central to the belt of constriction.

It may be that permanently enlarged muscle cells are less stable than normal fibre ; in any case, whether after previous hypertrophy or not, it seems that this coat is liable to the *fibroid degeneration*, or substitution, or fortification, which slowly establishes itself throughout our bodies and increases from youth to age. If less efficient it is less expensive. This diffuse fibrosis is of course distinct from the atherosclerosis of the intima, which may be diffuse or patchy. On a still lower level we find hyaline, fatty, and calcareous degenerations ; as in that mode named after Mönckeberg, and is not easily observed in the arteries of the

legs by x-rays and by the local disabilities to which it gives rise. The hyaline or insoluble colloid phase may often escape notice, but probably always precedes the fatty (see also Evans, *loc. cit.*). Thus, whether due to original poor quality, or to the effects of incident poisons, the media breaks down in spots and patches of fatty decay ; and, as this decay appears, bright points may be seen under the microscope where lime, attracted by the fatty acids, is deposited in the media, axially and often along its inner border, and as it accumulates, becomes visible under x-rays ; in extremer cases it encircles the vessel and converts it into a rigid pipe. This seat and kind of decay owes less to physical strain than does internal arteriosclerosis ; but as under the stresses of the circulation the whole vessel is stretched both lengthwise and crosswise, and gives way unequally in its better and worse parts, it is on each diastole thrown out of its bed, and to the eye is tortuous and unequal and hard to the touch. Such changes soon become apparent in the snaky folds of the brachio-radial artery at the bend of the elbow. I need hardly say that alongside this degradation of the tunica media the intima rarely escapes some affection, as in its turn intimal disease tends to affect the media, though in each case less than might have been expected.

Such, so far as the media is concerned, is the kind of change I have called " involutionary " or " *decrescent*," adjectives to which Dr. Geoffrey Evans demurs, as they seem to exclude infectious factors. Other authors of consideration are approving and using the term " decrescent ", and surely the senile factor is a

large and common one. The decay may be simply a senile deterioration, or relatively senile—the wearing out, in Osler's phrase, of tubing originally of poor quality ; or it may be, I admit, wholly or in part the traces or ultimate result of some past incident, infection, or flaw not essential to old age ; pathological, not physiological ; and so far, therefore, not to be called "senile". But the more the infectious coefficient, the earlier, as a rule, the incidence on the life. It is true, no doubt, that sometimes in subjects aged over fourscore we may find the arteries free from notable damage.

Now, although we are not to speak lightly of such damage to important subservient structures, yet, as a matter of practical experience, patients with vessels thus worn, if not subjects of excessive pressures, often live an active life of mind and body into far old age. Much depends of course upon the particular areas of arterial decay, which are far from uniform ; often the decay falls chiefly upon the larger vessels of the limbs ; and as the minor twigs supplying the voluntary muscles are not so subject to disease, the decay of a larger branch, so long as it is not choked, need not prevent a tolerable measure of blood supply, whether to limb or viscus. Indeed a vessel of which, under post-mortem examination, the channel seems obstructed or even occluded, under the pulsations of life may not have been quite impervious. In this kind of sclerosis the arterial pressures may be, and usually are, fairly within the limits of the normal. It is surprising to find how little these very conspicuous forms of arterial disease, medial or intimal, do of

themselves affect the blood pressures. With hyperpiesis we enter upon a different series of events.

Now let us turn to *the tunica intima*; this coat is liable to the disease called variously "diffuse hyperplastic sclerosis", "atherosclerosis", or, in the larger vessels, atheroma. Atheroma is a patch of so-called "diffuse" hyperplastic sclerosis, conspicuous by its seat upon the inner aspect of a vessel of some magnitude. So far as the microscope can tell, there is no histological difference between "diffuse" and patchy atherosclerosis.[1] For this reason the name "atherosclerosis" better indicates the essential identity. The process begins in the subepithelial layer along the line of apposition of the inner and middle coats where products of degeneration, primary or secondary to some previous inflammation, accumulate. I have said, and still hold, that the process arises in this line of apposition of the two surfaces, because this is a line of less resistance and of possible cleavage. At this junction slip and shearing stresses would set up molecular or massive lesions with slow and even hardly recognisable reaction—a very chronic "inflammation".

Again, in curved tubes stream lines break and the fluid continually changes its position with respect to the sides of the tube as the axial stream approaches them; then, where the angle diminishes so as to approach a right angle, the swirl becomes a closer and closer spiral, the tube wall is scoured, and there again may be slip of media on intima.[2] That atheroma appears at the sharper forks and branches is

[1] Evans, *loc. cit.*, and others.

[2] See also Cranston Walker, *Brit. Med. Journ.*, 1922, i. 260.

familiar to us all; however, I suspect that, a few angles excepted, such as the intercostals, the curves of our arteries are not acute enough to set up vertical motion, and that the adaptation of the blood stream to its vessels is become so consummate that the stream may be practically linear all through.

It is often assumed that under hyperpietic as contrasted with decrescent atherosclerosis the lesion is diffuse, the patches being decrescent. Not so; in hyperpiesia of standing enough for such damage the vessels are patchy, beaded or studded, intermediate lengths of the vessels being often translucent.

Chronic, very chronic, as in some cases atherosclerosis may be, yet Dr. Evans insists, as Klotz had done, upon its marks, or residues, of inflammation; although they never amount to or even approach the more abundant small cell infiltration of all the coats, such as we see in the definite inflammation of vessels ensnared in traumatic or tuberculous granulations, they signify, no doubt, attempts, however feeble and inconspicuous, at repair of a lesion—mechanical, or toxic, or both.[1] The yellow colour is due to cholesterol; as it increases it passes from the ester to the crystalline state. An excess of cholesterol in the blood is suspected rather than proved; I have said that the results of feeding rabbits with cholesterol are far from convincing.

Intimal decay is generally associated with changes in the inner elastic tunic; the elastic is multiplied; three or four bands of it appear for one; and, as we

[1] Klotz, *Journ. Med. Res.*, 1915, xxxi. 3; he insists upon toxic rather than mechanical causes; no doubt both are concerned.

see by their wavy folds, the resiliency of this fibre is impaired. Whether this be a true hyperplasia (Turnbull) or a splitting of the original coat (Jores, etc.) is undecided. Dr. Turnbull seems to give more weight to a hypothetical toxic than to mechanical detriment.

Now this subintimal disease—this atherosclerosis—may or may not be associated with high intravascular pressures—the so-called " hypertension ". That high pressures should affect the vessels after the manner described seems quite intelligible ; but in at least fifty per cent. of cases of atherosclerosis the pressures are not excessive, nor, as inferred from the size of the heart and otherwise, ever have been. Neither, in comparison of various cases, is any proportion seen between the extent or degree of the arterial changes in the same part of the same artery, the records of the arterial pressures during life, and the size of the heart. To this problem, however, we shall return later. A thickened artery, then, may be the seat of this intimal atherosclerosis, or of decay of the media, or of both combined. Not only are these thickenings very partial, and seemingly capricious in their incidence, but also they arise in vessels of various structure, as various as is the elastic aorta from a muscular arteriole, so that succinct histological description is not easy. Extensive atheroma may be found in the abdominal aorta, while in the thoracic it is absent or inconsiderable (p. 11). Perhaps under excessive blood pressures it is the finer ramifications that yield first ?—yet these may be protected in or by the belt of constriction. Observations of the finer vessels in recent cases of non-renal hyperpiesis are much to be desired ; but

necropsies in such cases are scarce. What we know is that in adults under fifty years of age, and in certain rare cases in children (Turnbull), high pressures may prevail for years—say four to six years in adults—without gross injury to the arch of the aorta ; or with no more than a moderate degree of dilatation.

I have contrasted (p. 7) the circulation in the blood-vessels with that in the periphery outside them, where in secret the intimate business of life is transacted ; in the workshop of colloidal, ionic, osmotic, and intersurface balances—in a word, of biological dynamics and reciprocal actions. Upon these tissue momenta the movements of the blood are largely dependent ; its tides will rise and fall in obedience to one, or all, or the algebraic sum of these coefficients. Here lie the sources of protoplastic dynamics, hidden rhythms behind the vasomotor or respiratory ; and on these rhythms and the purity of the fluids the integrity of the finest vessels may depend. But with these molecular activities the capillaries are most directly concerned.

Capillary pressures are often overrated ; the resistance of small arteries, of overlying tissues, and occasionally perhaps of slight œdema, may interfere with an exact record. They vary no doubt a little in different areas, but probably only about a norm of some 10-15 mm. Hg.[1] Boas and Frant report

[1] Hill, L., and McQueen, *Brit. Journ. Exp. Path.*, London, 1921, ii. 205. See also Danzer, C. S., and Hooker, D. R. ("Microcapillary tonometer", *Amer. Journ. Physiol.*, 1920, lii. 136); Boas, *N.Y. Med. Journ. and Med. Rec.*, 1923, cxvii. 528 ; and Boas and Mufson, *Journ. Lab. and Clin. Med.*, St. Louis, 1923, ix. 152; and Boas and Frant, *Arch. Int. Med.*, 1922, xxx. 40 ; and *Montefiore Hosp. Rep.*, vol. i.

capillary pressures of 30 mm. and over. Their volume and tides, if in part due to vasomotor action in themselves or in their arterioles, must yet depend largely upon the tissue hunger, the dynamic of protoplasm, the size of the corpuscles (the red corpuscles swell with a charge of CO_2), low diastolic pressure, and recoil waves wasting the pressure head in the central reservoirs and so increasing the work of the heart (see p. 39). It is difficult to understand how pressures can be measured in an area of network which has instantly alternative collateral channels. Nor is it easy to see how the capillaries could have " a propulsive function ", unless it were synchronised with that of the heart, which is not likely. That the capillary vessels are subject to morbid and extreme stony, and even to structural disease, as may be witnessed, for example, in the Malpighian tufts, seems certain ; they may widen and grow tortuous, or shrink and vanish ; and the stream may slacken even to stagnation. One would suppose that in disease their pressures would fall. Krogh says that they have a normal dilating capacity up to four times their radius. In cardiac defeat death may be directly due to stagnation of blood in the capillary bed.[1] It has been said (Boas and Mufson, *loc. cit.*) that in hyperpiesia the capillary pressure is low, in renal hyperpiesis high ; if so, this

[1] See H. H. Dale, various papers on histamine and congeners ; and Batty Shaw, *loc. cit.* Burn and Dale think that capillaries affected by histamine seem still to show constriction under some ill-understood conditions. Acetyl-choline simply relaxes the muscular arteries, with fall of peripheral resistance and increase of limb volume. The action of histamine on the capillaries seems to be of a more complex order. (Dale, *Brit. Med. Journ.*, 1923, i. 959, 1006 ; Burn, J. H., *Journ. Physiol.*, 1922, lvi. 232.)

feature is not quite homologous in the two series; but arteriolar constriction need not necessarily lessen capillary content and tension; however, we do not know enough about this subject to discuss it further at present. Direct observations of the capillaries, as at the roots of the nails, give very variable results, even in the same patient, and in several fingers of the same. But further observations are required and may be fruitful. Sir T. Lewis finds that in health the minute vessels of the skin can withstand internal pressures of 70-90 mm. Hg.

The morbid anatomy of *the "high pressure heart"* may vary as the incidence of some toxic influence in addition to sheer fatigue (p. 22). Sir Frederick Mott [1] well describes such a heart as "œdematous, almost sponge-like, the exudation separating the fibres, and sometimes small hæmorrhages. Moreover, the circumambient lymph is abnormal, carbon dioxide and fatigue products being in excess, oxygen in defect. The muscular fibres are lustreless, indistinctly striated, and studded with minute fat particles."

Speaking broadly, we should say that such a myocardium tells of extreme fatigue; for fatigue, or even strain, seems not to result directly in fibrosis, which supervenes rather on failure of the coronary circulation to supply good and abundant blood. The heart described by Sir Frederick Mott seems to have been "at the far end"; for often in fatigue cases the myocardium shows no very grave histological change. Indeed the large majority of such hearts are capable of a rally, if they get a chance; some of them do get a

[1] Mott, F., *Arch. Neurol.* i. 499.

chance and survive for a while. Intrinsic or coronary myocardial degradation belongs generally to a time of life beyond that of the hyperpietic group ; in old people the coronaries, and the left vessel especially, are rarely without patches of atheroma. Still even then, as in the analogous case of senile kidney (p. 57), they are often patulous enough to keep going so much heart muscle as the old man ordinarily needs. It is in persons of mid life or younger that arteriosclerosis is of ill omen.

Syphilitic disease of the myocardium is a rare event, but not therefore to be forgotten, especially if there be evidence of heart-block.

CHAPTER IV

Clinics

The names hyperpiesis and hyperpiesia seem, then, to be generally accepted ; the one as signifying simply the pathological coefficient of abnormally high arterial blood pressures, systolic or diastolic or both, the other a " disease " ; *i.e.* a particular series of events in the bodily system, concurrent and successive, positive and negative, repeating itself with fair uniformity. To call a disease an " entity " is medieval, and false. Are we to call health an entity ? Like disease, it is a state of an entity. For example, in the puerperium the arterial pressures may rise, a tell-tale phenomenon foreboding eclampsia ; or in " crises " they may rise and fall ; or in pain, as in a colic, pressures, the systolic especially, rise and fall according to the degrees

of it ; in certain renal diseases high pressures are more abiding. These incidental high pressures may be signified by the general term hyperpies*is* ; but the name Hyperpies*ia* signifies a certain disease which, independent of the kidneys, has its own characters, of which high arterial pressures, systolic and diastolic, seem to be the chief.[1] It may be that the disease, or run of morbid events, called hyperpiesia is a direct consequence of the mechanical strain, that the metabolic disorder may in itself be of a harmless nature.

The extreme limit of *normal* systolic *pressure* during rest we may take at 140 mm. Hg—though this, if persistent, is a suspicious degree—and of the diastolic 90 ; the mean adult pressures move round systolic 120 and diastolic 80 ; that is, the differential pressure moves around 40. For women the mean is perhaps a little less, especially during a menstrual discharge. Under physical and emotional disturbances, however, pressures fluctuate widely, but mainly the systolic. During adolescence the pressures tend to a slight rise ; in girls a little earlier, with their earlier development, but during the attainment of puberty—say from æt. 17 to æt. 22 (in boys ; three or four years younger in girls)—there is a slight remission of pressure, especially of the diastolic, in both sexes. In our undergraduates pressures often run low ; partly because their muscular exercises open out larger peripheral areas, pulmonary and systemic ; thus in the active undergraduate the systolic pressures may not exceed 110. Strictly speaking, we may assume

[1] See Batty Shaw, *loc. cit.*

that in middle life pressures may rise slightly, but normally not so much as is generally supposed.

There seem to be diurnal tides of pressure, probably vasomotor, even during the peace of night, which may explain the well-known nocturnal attacks of dyspnea, or of angina. They are no doubt dependent, at least in part, on visceral calls for oxidation. The fault need not be altogether "heart failure". Certain records made during sleep in healthy undergraduates (between 6 A.M. and 7 A.M.) were lower than in the same persons when again at rest in the forenoon (Michell).[1] Rest in bed may produce in the normal man a drop of 10-15 mm. Hg, chiefly systolic, in fifteen to twenty minutes; and even in hyperpiesis with large heart a week or ten days of bed nearly always brings down the abnormal excess by 20-30 or possibly 40 mm. Hg, presumably, as in diathermy, by vasomotor relaxation. Unfortunately, as the patient gets about, the pressures rise again. In these phases the diastolic pressure is the more significant. In auscultation I take the critical moment of diastolic pressure as, or just

[1] Allbutt and Rolleston's *System of Medicine*, 1909, v. 201. See also C. Müller, *Act. med. Scand.*, 1921, lv. 381. I have been much indebted to the many diligent records made by our late friend and colleague Dr. R. W. Michell in Cambridge. He secured the sleep records by attaching the cuff overnight and creeping to the bedside in early morning hours with the sphygmometer. Dr. Michell was killed by a shell fragment while bringing in wounded from the firing line. He had brought in five or six on his back before he was hit. Since these words were written Dr. Percy Stocks has published (Camb. Univ. Press, 1924) a larger statistic of pressures for age, and makes some calculations of heart values in terms of pressure and velocity. I fear the variables are too inconstant for control; *e.g.* some of Dr. Stocks's figures are higher than Dr. Michell's and mine; especially of mine in quite *normal* persons of middle and late middle life.

before, the fourth or "muffled" sound passes to silence. An intercurrent pyrexia usually reduces arterial pressures; and this fall may precede the indications of pulse rate or of temperature (Batty Shaw). A fall of pressures may usher in one of those terminal infections, such as pneumonia or influenza, by which hyperpietic cases are often brought rapidly to an end. On Dr. Batty Shaw's records some cases show "plateau charts", others remittent; in some occurred sudden drops—"hypopietic crises"—often with perilous symptoms; though in a few "it just went back again". A severe and perilous fall may be due to a "histamine effect"; that is, to accumulation of blood in the capillary areas, and slacker return to the heart. But from the unwary a small pulse (narrow radial) may conceal very high pressures, both systolic and diastolic. If a fall appears to be due to a yielding heart we may look out for trouble; a very gradual diastolic fall may signify only an increasing rigidity of the main arteries (p. 64).

It is said that arterial pressures of 160-170 are for some individuals normal; that "they are made so". I cannot deny this assertion, though I do not believe it; just as I cannot deny that some "normal persons" may have an action of the bowels only twice, or once, a week. The truth is that as high pressures creep on stealthily the system as silently adapts itself to them; so that blindly to try to reduce excessive pressures permanently to the normal would be as harmful in practice as fallacious in reason. However, the erring physician would probably find it difficult to carry out his intentions. Let the morbid state be modified

gradually and gently towards that mean level which experience must discover for each individual case.

It is not perhaps fully understood that, as we might have expected, abnormal pressures—whether high or low—prove to be less stable than the normal. This rule we must not forget when watching a case of hyperpiesis, lest we lay too much stress on fluctuations even so wide as 20-30 mm. Hg. This instability may account for the alleged increased sensitivity of hyperpietics to adrenin. Besides, with the rather rough estimations only open to us with gauges applied, however carefully, outside a vessel, we must not reckon on approximations closer than, say, 10-15 mm. either way.

That certain persons, by inheritance or otherwise, possess a "*hyperpietic diathesis*" may be; there may be in them a metabolic warp with a tendency to the formation or release of one or more pressor ingredients (p. 25); a tendency which may perhaps betray itself comparatively early in life. We know from inorganic structures, as by a change of refractive index, how a turn of molecular configuration will cause a swerve of the functional path.

Of the alleged periods of *hyperpiesis in children*, of my own knowledge I can say little; it is much to be desired that physicians engaged in school practice would carry out some researches on this subject. The cases of high pressure in childhood recorded by Dr. Evans, Dr. Sheldon, Dr. Hawthorne[1] and others, were for the most part, if not all, cases of contracting kidney. Notwithstanding, my own limited experience has been that rises of systolic pressure in children, not

[1] Hawthorne, C. O., *Practitioner*, 1922, cix. 425.

of renal or valvular origin, are not uncommon, but are transitory. The diastolic pressures in them are apt to be low, by reason of their very distensible arteries. What these phases mean, and whether or no they indicate a tendency in later life to take the permanent form of hyperpiesia, I cannot say. They may mean no more than a wider swing of the less settled structure of the child ; as, for example, in the larger respiratory rhythm of their circulation. But precise observations in young folk are difficult ; their resilient arteries give a relatively high systolic pressure, and fluctuate quickly and widely to changes of posture and emotional attention, even during the application of the gauge. Generally speaking, to quote systolic pressures only is fallacious. In normal children a widening differential pressure would generally suffice to interpret the swinging rhythm as a transitory phase.

In Professor MacWilliam's laboratory Melvin and Murray tested forty healthy children between the ages of 5 and 9 (by the auditory method). They found the pressures about the same as in adults, but the diastolic pressure a little higher, and accordingly the differential pressure a little smaller. As the contracted kidney is probably the tardy result of an infection, known or unknown, so the high pressures which it engenders may occur at any age, from 'teens, or younger, to scores. Hyperpiesia, on the other hand, the non-renal series of events, is a malady of riper years.[1]

[1] The rare cases of arteriosclerosis in children I need not discuss in this Lecture. I have mentioned them in my book on *Arterial Diseases*, 1915, vol. i. p. 171. See also Evans, G., *Quart. Journ. Med.*, Oxford, 1922–23, xvi. 33.

It is said that in women hyperpiesia is apt to set in about the climax of the menopause ; in this opinion I am disposed to agree, but we have to remember that the malady is apt to manifest itself in either sex at or soon after middle age—say æt. 50-65, usually after an unknown and no doubt often long period of latency. In our therapeutics it is unfortunate that by this stealthiness we are generally prevented from dealing with it in its incipience. If the hyperpiesis be due to menstrual arrest relief may be hoped for as the system recovers its hormonic balance.[1] Of this important issue the gynæcologist will judge best ; the general physician sees the cases in which recovery does not take place on these easier terms. If, as is said, during actual menstruation the blood pressure falls, this as a transitory symptom of depletion is not improbable. In both sexes in later life bouts of hyperpiesis are apt to occur (p. 60), and in the atheromatous are perilous. In one elderly atheromatous patient of mine such a reaction broke down the brittle aortic valve, setting up a permanent regurgitation. Syphilis apart, the comparatively rare instances of aortic regurgitation from atheroma may have this explanation.

To *palpation* the accessible arteries should hardly be perceptible before æt. 20, or in many persons even up to æt. 30. Thereafter they become palpable, and between æt. 50-60 more so still ; but this is not, nor need be, arteriosclerosis, unless the interpenetration

[1] See Moorhead, T. G. (*Med. Press and Circ.*, 1923, N.S., cxv. 316), who thinks extract of corpus luteum (p. 94) and "D'Arsonvalisation" helpful.

of a fine fibrosis (p. 34) be so called. Visibility depends of course much on overlying tissue ; but the radial, and the brachial at the bend of the elbow, may become visible under thin skins and in a cross light at ages from 30-35 ; and more and more so of course as age and elongation increase. In labouring men these signs may be seen sooner (p. 22).

How far does observation of the accessible arteries carry us towards an inference of the state of vessels in other areas ? Not very far. Boas has made some calculations of the probabilities, and says that only in one-third of the cases does accessible arteriosclerosis give a fair indication of this vascular disease in other and inaccessible areas : in other words, in two-thirds of these cases the disease exists out of sight and touch.

Let us now consider high arterial pressures and their consequences from four clinical *points of view* :

A. *In primary diseases of the heart* ;

B. *In renal disease* ;

C. *In hyperpiesia* ;

D. *In atherosclerosis unassociated with notable excess of pressures— Apietic Sclerosis.*

In (A) *Diseases of the Heart* we have many occasions to observe the imperious demand of the central nervous system, especially of the palæostriate centres and the bulb, for blood ; *coûte que coûte.* Professor Langley and Dr. Adrian tell me that even in the decerebrate animal the blood pressures are but little affected. On change of position they may vary but by a few millimetres only. Be the heart then well or ill, the supply must be forthcoming, and instant. Dr. H. J. Starling of Norwich pointed out that, embarrassed

as the heart may be by valvular or even by myocardial disease, the call is still relentless ; if the circulation be retarded the heart must draw upon its reserves ; to drive the blood through the periphery the arterial pressures in the proximal vessels must rise, or all go bankrupt together. It is wonderful in such straits what high pressures this gallant viscus can achieve—for a while of course ; and this not only when with a damaged valve there is a fair myocardium but also when the myocardium itself, big as in mass it may be, is far from its best. It is for this reason that in cases of hyperpiesis I have preferred to speak not of heart failure, but of heart fatigue and heart defeat.[1]

The demands upon cardiac energy are so wide, and often so sudden, that the coronary arteries must stand free of all sarcous investments ; but this is at the cost of the loss of such external support. Therefore these trunks, like the temporal, are the more prone to atheroma by distension. On the other hand their branches in the myocardium are often, perhaps by its protection, intact or nearly so ; as indeed we commonly see in intramuscular vessels elsewhere. However, clinically speaking, if the systolic pressure begins to fall while the diastolic is constant, or even rises, the heart is giving way.

In aortic regurgitation a big left ventricle may

[1] For discussion of rise in rate and pressure, both arterial and venous, in hyperpnea, and use of venesection, see Haldane, *Brit. Med. Journ.*, 1917, i. 181. Recent researches seem to point to a pressure centre in the basal ganglia and above this in the mid-brain—perhaps in the corpus striatum, and again in the cortex ; and that blood pressure does not influence the vagus directly, but through the mid-brain centre to which that in the medulla is subordinate.

force systolic pressures to a high degree while the diastolic may not rise, or may fall. We may witness such extremes as systolic 180 and diastolic 40, and not without anxiety lest the bottom drop out of the circulation; as indeed sooner or later it does: but meanwhile the low diastolic pressures give some relief to the arterial tension. In the late, even latest, stages of mitral regurgitation the systolic pressure may still trudge up to 200. But to pursue the subject of pressures in primary cardiac disease further would take us outside the limits of this lecture. But of the uræmia occasional in these cases I will speak presently (p. 64).

Let us now pass on to the persistent high pressures of (B) the *contracted kidney* and of (C) *hyperpiesia* respectively. These two concepts, separate as they are, I take together, as the first duty of the clinician will be to discriminate between them in the individual case: often an anxious problem. Professor H. Maclean [1] writes: "Although it is true that high blood pressure and hypertrophied heart too often mean chronic nephritis, yet there is now sufficient evidence to prove, quite conclusively, that in many patients with high blood pressure and other cardiovascular changes the kidneys may be slightly, if at all, affected". As this distinction is now recognised by testimony almost universal, I may take it for granted.

A patient is found to present, let us say, a systolic pressure of 220 and a diastolic of 180; to which of the two series does he belong? A specimen of the col-

[1] Maclean, H., *Brit. Med. Journ.*, 1922, ii. 181, 1069; Allbutt, *Diseases of the Arteries, including Angina Pectoris*, 1915, i. 378.

lected urine of 24 hours will be examined, and if the sp. gr. prove to be about 1020, or more, the diagnosis will lean towards hyperpiesia. Professor H. Maclean tells me that if the patient does not drink for 15 hours, and the first urine thereafter is tested for urea, a fairly approximate reckoning of *the renal capacity* can be made in a few minutes ; *i.e.* for the present accepting the urea concentration as an index. Normal kidneys may, it is true, have their moments of laxity or torpor ; but a diseased kidney, as of the contracted kind, cannot at any time excrete a urine of full value. Neither need a short salt delivery be the fault of the kidneys themselves. The discovery of some albumin in the urine, of a few hyaline casts, or even of an occasional epithelial or granular cast, need not disturb this presumption ; though of course in both these last respects the contracted kidney may also be negative. I think, however, that hyperpiesia patients, especially in the later stages of their disease, are liable to a superficial catarrh of the kidneys, possibly as one way of terminal events.

In the next place the blood also will be examined for its concentration of non-protein nitrogen, and if this fall within the normal range the presumption of hyperpiesia will be fortified. When Ambard first published his estimations of *non-protein nitrogen in the blood* the cases of hyperpiesia then under my care were thus examined, and in them we found no excess of urea concentration. Conversely, we found that a high concentration of non-protein nitrogen in the blood did not, of itself, set up high blood pressures. In the last stages of a very severe case of hyperpiesia,

with extreme symptoms, including two apoplectic seizures, Dr. Charles Wolf never found the urea concentration above 45 mg. for 100 gms. and this on a single occasion only. In another rather severe case, now under my care, we find that the concentration ranges about 38 mg. Many subsequent observers have obtained the same results [1]; so that in hyperpiesia the negative quality of the blood in this respect is fairly well verified.[2] Moreover, in these cases a low protein diet for some weeks seems to make no difference (p. 84); nor does a fall in blood urea coincide with fall in arterial pressures.

Indican is generally absent from the urine, or exists in faint traces only. It seems in chronic interstitial nephritis with high blood pressures that the bilirubin in the blood is a little under the normal; and Dr. J. W. McNee has suggested that an increase of it might prove to be a useful early sign of heart fatigue.

One or two recent writers seem disposed to revert to the notion that these cases of hyperpiesia are but early stages of chronic renal disease—especially of primary contracted kidney. The clinical physician knows better. He sees, on the one hand, in young as well as in middle-aged persons, the weariness, the headache, the gradual impoverishment of the blood, the sallowing of the complexion, the puffy eyelid, symptoms becoming more and more distinct as the glomeruli are successively attacked, and these sufferers he contrasts with the non-renal hyperpietics; active,

[1] See Rolleston, H., *Newcastle-upon-Tyne and North. Counties Med. Journ.*, 1923, iii. 71.

[2] See also Mosenthal, H. O., *Trans. Assoc. Amer. Phys.*, 1920, xxxv. 88.

well-coloured persons, free from nausea, headache, and all other symptoms of incipient uræmia. And in these it is that a blood examination reveals no excess of non-protein nitrogen. For a large and solid foundation for the differential diagnosis I refer the reader to Dr. Batty Shaw's book.

It is said that in hyperpiesia of high degree an excess of *sugar* may be detected in the blood. If so it must be an overproduction not an under consumption, as, whatever the diet, sugar does not appear in the urine of uncomplicated cases.

Eye Symptoms. — The retina must always be examined, and its phenomena scrutinised. If it present obviously the picture of renal neuroretinitis the response seems almost decisive ; yet the changes observed may be ambiguous. In either malady the arteries may be narrow, and opaque, bright or silvery ; or the arterial twigs may indent or kink the veins ; or the twigs may be beaded or corkscrewed ; or again, with or without all this, there may be a veil of œdema over the retina, and the discs rather congested and their outline confused. Even a hæmorrhagic, or possibly a white, spot, suspicious feature as it must be, may not testify decisively to a renal origin. In my experience a retinal hæmorrhage is not an uncommon event in pure hyperpiesia ; and, although the retinal vascular sclerosis may be permanent, yet if the other signs clear up, sometimes indeed rapidly,[1] the somewhat lighter diagnosis of hyperpiesia will prevail. Bardsley, raising pressure by means of adrenalin,

[1] See Bardsley, P. C., *Brit. Journ. Ophth.*, 1917, i. 239, and Batty Shaw, *loc. cit.*

was able to produce visible changes in the retina; and we are told by experts that in eclampsia to clear the womb of sepsis may rapidly disperse both high blood pressures and "neuroretinitis". Ellis and Marrack[1] seem to think that much of the retinal disorder may be due directly to high pressure; of their nineteen cases nine were chronic renal disease; ten hyperpiesia. The mean age in the former was 33, and these patients died mostly of uræmia; the mean age in the latter was 49, and of these there was no death by uræmia; three died of cerebral hæmorrhage, two of cardiac defeat; five were still living.

Mr. R. Foster Moore has published a very interesting study of *Retinal Venous Thrombosis* (1924) of which the outstanding cause is arteriosclerosis. Usually he observed a natural tendency to a restoration of the circulation by collateral channels, or by boring through the clot; but never to full recovery. Exudative patches and hæmorrhages may be seen in the retina; and irregular contraction of the field of vision. Nearly half of Mr. Moore's patients died of cerebral lesion; the duration of life after the thrombosis was 5-8 years. To illustrate their importance in a general diagnosis of this disease, Dr. Bernard Chavasse has recently exhibited lantern pictures of retinal changes in "arteriosclerosis," and on the whole agrees with Foster Moore. What the general physician now wants are estimates of the value of the retinal changes as a guide to those of the cerebral vessels.

Again, there is no parallel between general arterial pressures and intra-ocular pressure. Colonel R. H.

[1] Ellis and Marrack, *Lancet*, 1923, i. 891.

Elliot and Mr. Arthur Cooke are quite clear about their total independence. Colonel Elliot [1] says this is true for patients of all ages. Neither has general arteriosclerosis any bearing upon glaucoma. There is no excess prevalence of glaucoma among hyperpietics. Elliot mentions a case in which, while the arterial pressures were 200 systolic, 180 diastolic, the intraocular tension was normal.

It is said by Weiner and Wolfner [2] that in cases of high blood pressure the pupil on first exposure to light contracts at once, and then dilates again; although still under the light. They consider this reaction, when present, to be "pathognomonic of arteriosclerosis with high blood pressure" or at any rate to be of "undoubted clinical value"; and that it is almost constant. Although I have had this note by me for some years I am ashamed to say that I have too often forgotten to apply the test and can give no decisive opinion about it.

The *Senile, Atrophic,* or *Arteriosclerotic Kidney* must be distinguished from that of chronic Bright's disease. The senile kidney may be full-sized and fairly smooth. Some years ago Professor Lorrain Smith [3] and I read a paper on this distinction which my colleague illustrated by an exhibition of fifteen specimens. This renal deterioration is no more than one area of a general atherosclerosis. As we know how remarkably the kidney tolerates gradual ablation of substantial

[1] Elliot, R. H., *Glaucoma,* 1918; Cooke, A., letter to me.

[2] Weiner and Wolfner, *Journ. Amer. Med. Assoc.,* 1915, lxv. 214.

[3] Smith, L., *Brit. Med. Journ.,* 1912, ii. 1273; and Allbutt, C., *Diseases of the Arteries,* 1915, i. 334.

fractions of its substance, so we infer that by atherosclerosis of its vessels patch after patch of the organ may be starved without seriously affecting its everyday functions ; though no doubt the reserve against unusual demands, as for example, of a major surgical operation, is reduced ; the total functional capacity is less. Still for years in these atrophic cases there may be kidney enough left for the more tranquil life of old people ; and arterial pressures do not rise notably. Moreover, it is suggested, or by certain histologists declared, that sounder parts, where the vessels happen to keep more pervious, may hypertrophy. Professor Shaw Dunn [1] supported our distinction between the mere atherosclerotic kidney and the primary contracted kidney, even although there may be some fibrosis of the cortex ; so does Boas ; [2] and so may other authors likewise. But probably under the blight of a past infection intermediate states may occur. Dyke [3] points out in the senile atherosclerotic kidney the absence of any traces of inflammation, present or past. The name " arteriosclerotic kidney " is better avoided, for renal arteriosclerosis occurs under at least three different forms : (1) Arterioles and glandular elements both affected by some infective cause ; a local disease : example primary contracted kidney. (2) Arterioles damaged by long-continued high pressures, hardly affecting the glandular elements ; a general disease : example hyperpiesia. It is probable

[1] Dunn, J. S., *Brit. Med. Journ.*, 1922, ii. 1166.

[2] Boas, E. P., *Med. Journ. and Rec.*, 1924, cxx. supplement, 169.

[3] Dyke, S. C., *Quart. Journ. Med.*, Oxford, 1922–23, xvi. 1.

that in hyperpiesia all fields are not contemporaneously under constriction but variably ; in some alternation or vacillation. (3) Arterioles sharing in a general vascular decay with other parts of the body resulting in merely atrophic effects on the glandular elements, reducing reserve but not perverting function : example " senile " kidney.

The *subjective symptoms in hyperpiesis*, renal or non-renal, are too vague for differential diagnosis in the early stages when we so sadly need the warning. In both diseases indeed the mischief may advance furtively until it has become irreparable, and hardly ameliorable. Of hyperpiesia it has been said that the majority of its victims " do not suffer from it " ; or the subjective symptoms may be consistent with some passing disorder. The protracted initial period of hyperpiesia has been named " presclerosis ", a meaningless if not misleading term. The vascular strain is surely not of the essence of the disease, but a secondary feature of it.

The subjective symptoms then, in their earlier period, are vague ; though perhaps always in the renal disease they set in earlier, and are more disturbing. Both kinds of patient may complain of some depression of spirits, especially of a morning (a healthy person tires towards evening), of languor, apathy even to torpor ; fatigue ; vertical headache, or fullness or weight on the head [1] ; insomnia ; beating of the heart, especially felt at night on the pillow :

[1] Dr. James Collier says that high pressures are not found in neurasthenics (*Brit. Med. Journ.*, 1924, i. 524). Such is my experience also.

in the hyperpietic such discomforts may be relieved by a blue-pill ; not so with the victim of renal disease in whom the symptoms are " uræmic " and prone to go on to nausea, morning sickness, sallow complexion, puffy eyelids, spasmodic dyspnea, and so on. On the other hand, a clear ruddy complexion and aspect of health and even the full sense of it are quite consistent with many a year of hyperpiesia.

It may be, in certain persons who suffer intermittently from phases of indisposition, that periods of high arterial pressure occur as part of some obscure metabolic perversion, or transient toxæmia. A study of such phases might be helpful in our search for the causes of hyperpiesia ; but they are hard to catch. The general practitioner would do well to take the blood pressures in cases of recurrent headache, " biliousness ", " suppressed gout ", restlessness, insomnia, clouded temper, and so forth.

Dyspnea—a little panting on hills or stairs, moderate in severity and felt only on ascents, is often mentioned as a first or early symptom of high pressures ; " heart tests " perhaps are made and, even if somewhat adverse, still too often the physician supposes that by its first notable manifestation he has detected the malady in good time. But no : dyspnea, however slight, means that the patient, whether renal or non-renal, however unaware of ill-health he may have been, has entered not now upon the first but upon the last stage of his malady. The spasms of dyspnea, commonly but erroneously called cardiac or renal " asthma "—the mechanics of asthmatic dyspnea are radically different—are of course of still worse

omen. Papp and Schurr of Vienna state that ordinarily in high pressure cases the plethysmographic curve (arm) rises gradually, but on or just before one of these panting seizures rises rapidly. But in ordinary hyperpiesis a moderate dyspnea on exertion indicates that the returns of venous blood to the right auricular system is abnormally rapid ; the heart has overdrawn its account and is slow in dealing with the rapid returns of venous blood to the right auricular system ; little savings may postpone a total failure, but the organ is no longer solvent.

A sudden oppression of cardiac dyspnea, as on walking uphill, is too often called " angina pectoris " ; a radical error ; generally speaking in angina the breathing is checked.

Of the current " *cardiac tests* " I can say little. These responses depend upon too many variables ; they vary even in the same person from day to day, with the general sense of hope and wellbeing, the psychological coefficients—such as a strange doctor, the habits and training of the individual, his chest expansion, his splanchnic tone, and so forth. Indeed to be set upon any exercise or chamber gymnastic to which the patient is unaccustomed, makes an irregular demand upon his energy. As a rough test in the consulting-room the patient may stoop and rise quickly some dozen or score times, when the systolic pressure should rise about 20 per cent. and subside in about ten minutes. If the pressure should fall instead of rising the forecast is bad. If the systolic rise out of proportion to the diastolic pressure, the arteries, the aorta especially,

are probably dilated beyond their elastic limits. We are all familiar with the large, thick, and jerky radial pulse of old men. In apietic cases and in aortic regurgitation the diastolic pressure may fall nearly, or quite to zero ; in hyperpiesis never—nor near it. The electro-cardiogram is of no service as a test of cardiac potential.

Cardiac Signs.—The physical signs of cardiac hypertrophy and dilatation are too well known for me to detain you by a description of them. I must be content to allude to long slow systole ; a second aortic sound accentuated, high-pitched, almost interrogative in its snap ; a gallop rhythm perhaps, or a duplicated first sound. Fahr[1] states that by raising the resistance the work of the heart, *caeteris paribus*, is increased nearly four times that called forth by a larger output per minute. Marey's principle of an inverse relation between heart rate and blood pressure may be broadly true, but is often submerged under contingent conditions. The pulse rate in high arterial pressure—say over 180—is usually somewhat accelerated, especially in women ; but under a sudden rise in pressure the pulse may be retarded by vagus action which checks the " pacemaker ", or, if extreme, may damp the conductivity of the *a-v* bridge also.[2] There may be some thyroid disorder amongst such cases ; in most of them the waves come unequally through the cuff, whether the irregularity be due to vasomotor, psychic, respiratory or vagus coefficients.

[1] Fahr, G. E., *Journ. Amer. Med. Assoc.*, 1923, lxxx. 615.

[2] See Eyster und Hooker, *Zentralbl. f. Physiol.*, Leipz., 1907, xxi. 615.

Dr. Stacey Wilson tells me he has observed in heart tone a property of transmitting or damping the vibrations of clinical percussion on the cardiac area ; that as a heart loses tone the normal percussion note on the chest clears as the resonance of lung or stomach comes through ; on the other hand normal or increasing tone absorbs more and more of the vibrations, and the note is dull. But in working out this problem a good many variables will have to be taken into account.

On the cardiac aspect of non-renal hyperpiesia, we must scrutinise the hackneyed diagnosis of so-called " *chronic myocarditis* "—a misleading term we should be far better without ; while of course remembering not to lose sight of possible infections ; for a patient may, and too often does, suffer from more than one kind of disease at a time. Furthermore, the coronary arteries may be decaying (see p. 43).

Fahr's large Insurance experience (*loc. cit.*) convinces him that " in the United States at least 50,000 persons per annum die of these hyperpietic hearts ; more than of apoplexy or angina ". I saw the other day, with Dr. Hall of Caxton, a lady suffering from dyspnea and a much-dilated heart, with auricular fibrillation. Her kidneys were doing well enough ; but her blood pressures were 200/130. Active woman as until a few days before she had been—she had been to church as usual on the previous Sunday—yet she had been drifting almost imperceptibly into a late stage of hyperpiesia. Even with the onset of fibrillation no fall of pressure had occurred, except perhaps the diastolic. In these stages of the malady much

patching may still be done, with digitalis and otherwise ; but the prognosis is not bright. Our principal guide must be the systolic pressure ; if this begin to fall out of proportion to the diastolic (Fahr mentions a case in which it fell by degrees to 140) the heart is bankrupt. Mosenthal [1] also believes that in hyperpiesia more than half the patients die of cardiac defeat ; apoplexy taking the second place in frequency ; but in hospital statistics it must be remembered that admissions for cardiac distress would be more than for apoplexies, many of which are rapidly mortal, or less easily admit of removal from home. In this manner hyperpiesia and contracted kidney may alike become " cardiac cases ".

I desire here to lay stress upon the *uræmia* which may arise in both of these maladies—in hyperpiesis with and without renal disease—but with a crucial difference in import. It is not generally realised that uræmia—severe uræmia, even, as I have said, with some neuroretinitis—is no very rare event in cardiac disease with renal disorder, as many a necropsy has proved, no deeper than congestion, and with good chance of restoration ; even after attacks more than once repeated. If, *pace tanti viri*, I may dare to say it, I think Dr. Batty Shaw has hardly realised the more superficial nature of this inter-current uræmia in cases of hyperpiesia in which the kidneys may be capable of substantial restoration. We may set the cardiac kidney over against the renal heart. For instance, in Dr. Shaw's 24th case [2]—one of high

[1] Nelson's *Loose-Leaf Living Medicine*, iv.
[2] Shaw, H. B., *Hyperpiesia and Hyperpiesis*, 1922.

pressures, dilated heart and pleural effusion—an outbreak of uræmia seemed to compel a diagnosis of contracted kidney. Yet in this and some other such cases (as for example the case on pp. 126-7 presumed to be "granular kidney") he had been surprised to find on necropsy, including microscopical examination, the kidneys reported as hardly abnormal. In this particular case (the 24th) the glomeruli were normal up to 96 per cent.; and the interlobular arteries but slightly affected. So again with another case of uræmia, with convulsions (p. 137), "granular kidney" was diagnosed; but on necropsy the kidneys weighed 6 and 7 ounces, and though deeply congested were smooth on surface; there was little tubular catarrh, and again 96 per cent. of the glomeruli were normal. Now in these cases the uræmia is an episode; and in the majority of them a first or even a second attack may be cured, or pass away.[1] Although this lecture is but a summary, I am tempted, for its large illustrative value, to quote a case recorded by Dr. Calvert of St. Mary's Hospital [2] in an able paper on our present subject.

Hyperpiesia

Case IV.

H. W., aged 56, suffering from violent headaches, recent failure of eyesight, general debility, and occasional well-marked nocturnal dyspnœa. Heart: left ventricle much hypertrophied; no evidence of valvular lesion. Arteries thickened but not tortuous. Blood pressure 230/134.

[1] See also Josué et Parturier, *Les Cardiorenaux*, 1921.
[2] See Calvert, E. G. B., *Brit. Med. Journ.*, 1925, i. 64.

Blood urea 0·051 per cent. Retinal arteries very sclerotic, discs a little fluffy at the margins. Wassermann reaction negative. Urine : 60 oz., specific gravity 1008, trace of albumin. Range of urea concentration = 4·4/0·9.

Practically the same results were secured just before death, which took place seven weeks later and was due to cerebral hæmorrhage. Transitory mild convulsions and delirium occurred in the third and fifth weeks and lasted six and thirteen hours respectively. *Post mortem* the kidneys revealed no appreciable abnormality beyond considerable sclerosis of their arteries.

The wide range of function had clearly distinguished the condition from that of chronic interstitial nephritis. Similarly, another case was differentiated by a range of 1·5/0·4 ; the blood urea was 0·045 per cent.

The influence of failure of the circulation on the test must always be borne in mind.

If we realise—say in a patient admitted to hospital whose former history may be almost unknown—that in a state of uræmia with large dilated heart we need not surely infer " granular kidney ", we shall undertake the cure with better hope. The condition, menacing as it may be, under prompt treatment will generally subside ; more probably of course if it be the first attack.

In the *toxæmia of pregnancy* the rising blood pressures offer the best warning of this peril ; scanty urine the next best ; and of less value albuminuria. Irving[1] reports that of such patients those with a pressure of 130-140, only one in thirty-two became toxæmic ; of those of 140-150 one in eleven ; of those of 150-160 one in three, and of those of 160-170 one

[1] Quoted by Bourne, A. W., *Brit. Med. Journ.*, 1920, i. 727.

in two. In severe eclampsia cerebral hæmorrhage was often the cause of death (Bourne).

Of other symptoms I would put in the next place the incidental and often *large hæmorrhages* of high pressures, whether renal or non-renal; to me indeed they seem more frequent in hyperpiesia, perhaps because I see a larger number of these cases. A person, who may not have become aware of any fault of health, is suddenly attacked by profuse epistaxis, or menorrhagia, or hæmoptysis; possibly indeed by hæmaturia or hæmatemesis, though these two last and rare events may be of doubtful interpretation. Dr. de Havilland Hall[1] has narrated histories of hæmoptysis in five such cases, and quoted four more, probably of this nature, from Andrew Clark. No. 1 had epistaxis (died of apoplexy): No. 2 likewise had epistaxis: No. 3 epistaxis (had also a hæmorrhage into the retina, and ultimately died of apoplexy): Nos. 4 and 5 had several hæmorrhagic attacks. In one of the patients inhalation of amyl nitrite stopped a hæmoptysis. In all these cases systolic pressures ranged variously from 180 to 230 mm. Dr. G. Evans thinks that these hæmorrhages break forth in districts of the body where the vessels are already advanced in disease, and are therefore the more alarming, as signs of extensive vascular detriment. This is only too true of apoplectic hæmorrhage; but I feel sure that epistaxis and hæmoptysis may break out in some, or in entire, independence of local vascular disease. Epistaxis—the most frequent of them—we know is apt to spring

[1] Hall, F. de H., *Lancet*, 1915, ii. 329.

from normal noses ; and disease of the finer vascular network of the lungs, apart from pneumonic or embolic accidents, does not seem probable. I look back upon several cases of pure hyperpiesia in which sudden and profuse hæmoptysis occurred, often more than once, yet in which remedies proved successful, and health and activity were restored for years, in two or three indeed (up to now) in full. These hæmoptyses may of course arise not in the pulmonary network but somewhere in the larger air passages ; they are a bright red in colour, or so one is told. In cases of atherosclerosis without high pressures such incidental hæmorrhages do not happen. In them also hæmorrhagic apoplexy is as rare as in the hyperpietic, whether renal or non-renal, it is frequent. Yet the three cases of death by coronary hæmorrhage into the pericardium which abide in my recollection were all cases of apietic atherosclerosis. Melæna is reported on good authority in some cases of high pressure, but to exclude other causes might be very difficult.

In the *Lancet* of Dec. 22, 1917, Professor Arullani of Turin is quoted as the describer of certain degenerative changes in the *vessels of the skin* in old age, natural or premature. He finds arteriolar dilatations, or small aneurysms, apt to rupture with punctiform hæmorrhage into the skin. He regards these changes as even an early sign of arteriosclerosis. All three arterial coats are affected, the media perhaps chiefly. These are presumably homologous with the cerebral " miliary " aneurysms. I have never seen them, but one does not see what one has not looked for.

Of *angina pectoris* here I will say little; I have dealt with it fully elsewhere (*Diseases of the Arteries*). I have stated over and over again that in the majority of cases of angina the arterial pressures are not increased. Linn Boyd, who has collected records of 5000 cases of thoracic aortic aneurysm, reports [1] that although high pressures are recorded in a certain percentage of cases, the incidental high pressure of some efforts played a far more important part. Naturally, however, by hyperpiesis the pain is aggravated; and indeed, by the stresses of it, the aorta may be so strained as to set up angina: but in practice I have found the high-pressure angina cases less tyrannous, because more susceptible of mitigation or cure, than those arising under ordinary pressures. Angina is not very often the way of death in hyperpiesia; usually death is an epiphenomenon, and relatively accidental. Three or four years ago a patient of mine, for many years the subject of hyperpiesia, during a time of exceptional work and care had a severe and typical attack of angina which awoke him from sleep during the night. By stricter rest and other hygienic precautions since his pressures have been better controlled, the angina has never returned, and he has been enabled to carry on his professional duties up to this day. Boyd agrees with me that anginoid pain—as contrasted with pressure pains and those of rupture—belongs to the early stage of aneurysm of the arch, and is "practically indistinguishable from angina pectoris"; that there are no differential symptoms, so that differential

[1] Boyd, L., *Amer. Journ. Med. Sci.*, 1924, clxviii. 654.

diagnosis is very difficult. Well it may be; it is impossible; the conditions are identical.

Once more, the subject of hyperpiesis may, as I have said, live happy, useful, and apparently healthy days over many a summer; and then be stricken down in the midst of them by an *apoplexy*. A main gable has collapsed, as if by a sudden gust; but the medical sapper can tell of a long insidious mining before the buttress gives way. Yet not infrequently signs of ill omen precede the stroke. For example; of sinister symptoms in hyperpiesis, whether renal or simple, or again in degenerative and thrombotic atherosclerosis, without high pressure, those of worst augury are *slight and often transient palsies*; in the two former diseases probably due to small hæmorrhage from some cerebral vessel, in the last to occlusion of it. Without vertigo perhaps, or other concurrent symptom, the patient during conversation may suddenly find himself embarrassed in his articulation; or clumsy with one of his hands, may drop knife or fork at a meal. He may try to put the interruption off by some effort or diversion, or, to avoid observation, may walk out of the room. And in a day or two, nay in a few hours perhaps, the fault may disappear. These patients, especially in the non-renal hyperpiesia, may suffer from several repetitions of slight attacks of this kind; some of them not going beyond a passing vertigo. Certain sanguine pathologists put these and such symptoms down to a transitory spasm of the cerebral vessels; a plausible opinion which I have contested.[1] The two vital organs, the brain

[1] In my *Diseases of the Arteries*, 1915, vol. i. p. 416.

and the heart, are mercifully not entrusted with much vaso-constrictive property, even when these vessels are healthy. That arteries impaired by decay are the more liable to "spasm" is a strange guess, for which there is no evidence of any weight. Reeves[1] records some interesting cases of disorder which he is disposed to explain by vascular spasm. But verification of spasm in individual cases is almost impossible; our evidence is of hæmorrhages; and Reeves has to admit that such morbid vascular spasm is very rare. Even in intermittent claudication a failure in supply of blood to meet a larger demand is a sufficient explanation. A no less fictitious explanation, now dismissed, was "patchy œdema". It is fair to admit that the spasm hypothesis has received some support from a few descriptions of spasm of the vessels of the retina. This phenomenon, however, is very rare; the last published example perhaps is that carefully recorded by Brauer in a man æt. 34. He had repeated attacks of blindness without any obvious pathological cause; the arteries and retina seemed normal until they were observed to shrivel up during an attack; after the attacks the fundus became again normal. The attacks soon ceased, and did not recur. Of course no one denies that arterioles may close in spasm, though one hardly expects this of hardened vessels, still less of vessels so poorly endowed with vaso-constrictors as the cerebral.[2] But the records

[1] Reeves, R. G., *Med. Journ. and Rec.*, New York, 1925, cxxi. 1.

[2] Recent research, by Drury and others, indicates that the coronary arteries at any rate are more subject to vasomotor activity than has been supposed; that they constrict readily under sympathetic stimulation and adrenalin, and dilate under

of the necropsy table offer a far more definite and adequate explanation. Dr. Geoffrey Evans agrees with me that, at least in the large majority of cases of high arterial pressure, these trips signify small cerebral hæmorrhages. In necropsy of such cases remnants of these hæmorrhages are generally to be found if carefully searched for; the old ones may be no more than yellowish stains, or a group of hæmatoidin crystals; the more recent distinct as spots of hæmorrhage. Generally speaking, accidents apart, these patients die, sooner or later, of hæmorrhagic apoplexy.[1] As pathologists then, in the necropsy of a cerebral hæmorrhage, we must not be content to point out only the obvious seat of the fatal stroke; a more assiduous search will often reveal traces of earlier and smaller ruptures. In another case of my own, one of high pressures of long duration, the patient, who enjoyed good health on the whole, and was active in public life, had yet been subject from time to time to slight vertiginous and paretic attacks. Ultimately he died of a fatal apoplexy. Besides the recent clot, we found marks or traces of fifteen others. Ellis,[2] in 31 apoplectic brains minutely examined, and sections made, found hæmorrhagic foci and

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vagus or pituitary stimulation, and under histamine. It is interesting to learn, however, that constriction of the systemic vessels by pituitrin is compensated at once by a dilatation of the coronary. Irritation of the sympathetic dilates the vessels of the brain, as in other viscera of the parasympathetic.

[1] It is hardly necessary to say that such repeated hæmorrhages may occur also under other conditions; *e.g.* purpuric, leukæmatous, gummatous, and sometimes in apietic atherosclerosis.

[2] Ellis, A. G., *Publications from the Jefferson Med. Coll. and Hosp.*, Phila., 1915, v. 1.

pigmented scars, many or few, ranging from 50-100 microns to several millimetres; some of course much larger. Some clots surrounded the ruptured vessel, others were confined to the perivascular spaces. "Miliary aneurysms" may or may not be present in such cases; they are inconstant and of no considerable pathological importance.

There is no need then to invoke arterial spasm. Indeed such vessels hardly could close down on their content. The critical moment of sanguineous apoplexy is a certain fragility of cerebral vessel with a certain height of the arterial pressure which has brought about the fragility. I have quoted Professor MacWilliam on the relative rarity of sanguineous apoplexy in aortic regurgitation; the heart is huge enough, but the mean arterial pressure is not much increased; in the brain perhaps hardly at all. However, as I have said, in these cases the mean age of the vessels is younger.

When in the apietic and thrombotic mode of atherosclerosis the cerebral vessels are failing, besides or before these smaller pareses, we may note vertigo, somnolence, fretfulness, some loss of memory, some incoherence of mind, some slurring of the feet or a drag of one of them; or like evidence of neurovascular atrophy of the brain. "Senile" epilepsy is perhaps always of atherosclerotic origin, not hyperpietic.

A long experience suggests to me that, not only is hyperpiesia an hereditary malady, but so also is the disposition to its particular consequence of cerebral hæmorrhage, as contrasted with the cardiac mode of death. In respect of age, a few cases of apoplexy

occur between æt. 40-50, but probably these are nearly all renal; then there is a rapidly increasing number between æt. 50-60; up to the heaviest incidence between æt. 60-70. In a family of old friends of mine, well known to me during three generations, nearly all the men—six or seven of them at any rate, brothers and cousins—were carried off in this last decennium of life by hæmorrhagic apoplexy. They were robust ruddy men; keen sportsmen who took hard exercise in the open air. They lived well, and took their glass or two of port after dinner, but by the standard of their day, were not intemperate. It is no rash inference to presume that high arterial pressures were prevalent among them—that as a family they inherited a tendency to hyperpiesia, and in this to cerebro-vascular rather than cardiac breakdown. I have noticed the same proclivity in many a family since, though not with such wide and intimate a knowledge.

There is before us, when face to face with an instant case of cerebral hæmorrhage, a certain very important and yet difficult pathological problem; it is this: if the majority of hæmorrhagic apoplexies are the results of prolonged high arterial pressure, yet of course this is not so with all. The apietic atherosclerotic cases of stroke, due to silting up of vessels, are usually distinguishable by other symptoms; for instance by the lenity of signs of cerebral compression during and after the seizure; there may be confusion only, a bewilderment less than coma; even though the palsy may be a heavy one. However, let us suppose a case in which the hæmorrhagic nature of

the stroke is clear : we shall probably find the arterial pressures high ; as we know, the substriate and medullary centres imperiously demand a reinforcement of cardio-arterial pressure, aided perhaps by a gush from the adrenals, to contend against the intracranial anæmiating pressure ; and to meddle with this temporary readjustment is a perilous undertaking. Remember a large heart may be yielding although still putting up a pressure of 200, and, as Professor T. R. Elliott says, the adrenals are soon exhausted ; moreover the local injury need not be hæmorrhagic but a retardation with thrombosis ; for as we know by electrical stimulation, irritation of the central ganglia of the brain produces a retardation and reinforcement of the heart's action (Luciani, Head, and others). Now the family physician, having more knowledge of the previous conditions to guide him, might decide at once to let blood ; but the physician who is called to an unknown patient in hospital may well prefer to wait and see. He will carefully examine the heart, its dimensions and sounds ; if these do not signify hypertrophy he will hold his hand ; for a labouring heart, vascular constriction, and high arterial pressure may mean only a temporary, a critical, response ; and if so little attempt should be made to moderate it. But in the next case of apoplexy and coma we might find, with thickened arteries, a previous history of systolic pressures over 200 ; tight aorta and carotids, a pulse perhaps under vagus retardation,[1] a twenty-ounce heart, and renal function

[1] In practice pulse rate and arterial pressure do not run parallel (see p. 62).

virtually normal; in cases such as these venesection may well be advisable; the big heart may carry on. In a simple case of intracranial hæmorrhage from trauma high arterial pressure would be wholly compensatory, and be respectfully let alone; decompression by other means being then the proper course. Lumbar puncture in these cases generally reduces arterial pressure, but the effect is transient[1] and negligible.

In an analysis of 65 cases of cerebral hæmorrhage, collected by pupils of mine in necropsy departments, those with granular kidney amounted to 65·5 per cent.; with normal kidneys 37·5 per cent. In 52 of the 65 the heart was hypertrophied; normal in 12. As a general rule in necropsy the state of the arteries of the base may be taken as a fairly good indication of the state of their intracerebral ramifications.

Many years ago, when investigating syphilitic disease of the cerebral arteries, I found it difficult to compare the smaller cerebral vessels with those of the same order elsewhere; they are so thin that it may not be always easy to distinguish media and intima; and one sees how small increases of external encephalic pressure must flatten and empty them; and, conversely, that they must be very vulnerable to increases of internal pressures. Neither in the lesser twigs is it always easy to discriminate between intimal atheroma and a bad media; moreover the intimal disease is apt to invade the media, though not so quickly and thoroughly as might have been

[1] See Gray, H. T., and Parsons, L., *Quart. Journ. Med.*, Oxford, 1911–12, v. 339.

expected. But that the process of intimal atherosclerosis prevails is obvious enough in the vessels of the base, where it stands out against the thin, pink, and almost translucent normal portions. Dr. Turnbull[1] agrees, however, that the degeneration does begin in the usual sub-intimal area, and that the dilapidation of the media, so far as there is a media, is consequential.

Sir Frederick Mott has warned us that in elderly persons, who are by no means immune to epidemic encephalitis, it may be difficult in certain cases to distinguish between the sequels of this disease and cerebral arteriosclerosis with decay of the mesencephalic ganglia, athetoid symptoms, and so forth. And the "Parkinsonism" may be encephalitic or the "real thing".[2]

Drs. Ll. Llewellyn and A. B. Jones[3] find a close association between "*fibrositis*" and arteriosclerosis, closer than a coincident age liability would account for; that "arterial disease is a feature of fibrositis". It is quite reasonable from analogy to suppose that a short supply of blood to the muscles might lead in them to fibrotic atrophy.

Upon the file of materials for this Lecture I collected the notes of a few typical cases of arterial disease in the several maladies in which it is found; but as by the side of Dr. Batty Shaw's book any collection of mine would be insignificant, and as hyperpiesia, primary contracted kidney, apietic atherosclerosis, and so forth are now well distinguished

[1] Turnbull, H. M., *Quart. Journ. Med.*, 1914–15, viii. 201.
[2] Mott, Sir F., *Practitioner*, 1924, cxiii. 244.
[3] Llewellyn, R. Ll. T., and Jones, A. B., *Fibrositis*, p. 125, 1915.

and known, it seems unnecessary to burden these pages with casual records merely to illustrate an accepted classification.

CHAPTER V

Prognosis

Prognosis is for the most part implied in what has gone before. When excessive arterial pressures are discovered our first endeavour, after disproof of syphilis, will be to distinguish hyperpiesia from *chronic renal disease*. The pressure register may be as high in the former as in the latter. The prognosis in the former case is more hopeful and the disease far less burdensome; and if by some chance—say by a slight substernal oppression (tight aorta) or an epistaxis, or again by an examination for insurance—the condition be discovered in fair time, which, however, in the absence of early subjective discomforts rarely happens, then, if the case be watched and judiciously managed, the outlook may be quite hopeful, especially in the obese (p. 19). Moreover in many persons, even in the quite elderly, phases of high pressure occur which prove to be transient; though probably recurrent. Much will depend on the biochemical reports on the blood and the urine, and on the course of diastolic pressures: diastolic pressures round about 100 are of ill omen. Response to treatment, on the other hand, is a favourable sign. The peril lies in the bigger incidents; in cardiac defeat, or apoplexy, or pulmonary œdema. If, how-

ever, the high pressures prove to have a renal origin the prognosis is more sinister, both as to suffering and duration of life. On this only too well-known alternative I need not dwell. Of course any incidental complications will have to be taken into our reckoning, and these are far more perilous in the renal cases.

Non-renal hyperpietics bear surgical operation fairly well; the renal very ill.

In the non-pressor (apietic) or "degenerative" cases of atherosclerosis the outlook may be hopeful, for many of these patients live to a good and even efficient old age; others unfortunately drift into sundry atrophies. In them prognosis depends on factors hard to ascertain; especially on the seats of the degeneration; whether, for example, in the coronary or in the cerebral vessels; or, again, in the larger rather than in the finer arborescences. Marked failure of memory, lapse in speech, slurring of the feet in walking, are of ill omen, at any rate as regards the faculties, but not necessarily so as to the duration of life. But under such adversity long survival may be no blessing. Finally, as we have seen, it would seem that many persons undergo more or less transient phases of high pressures, and recover, in happy ignorance of both doctor and disease; but these storms may account for some of the graver accidents or issues of primary atherosclerosis (p. 67). It is well therefore even in apietic cases not to forget to keep some supervision over the blood pressures, especially in the presence of symptoms of ailment.

CHAPTER VI

Therapeutics

And now, concerning the purpose of all this discussion; what is to be done? I wish I could speak more confidently of our power of healing in these diseases. Unfortunately for timely and therefore effective treatment I have to repeat that by far the majority of persons in the earlier stages of hyperpiesia "do not suffer from it"; indeed for a while they may feel even more active and better for a richer supply of blood to the brain. Probably the cerebral vessels, being but sparingly endowed with vasomotor energy, are not an area, or main area, of constriction; and so under high pressures may be the more liable to injury. It has been proposed that every man should be tested every five years, and our blood pressures and so forth recorded. This rule would indeed set up an epidemic of fidgets.

Into the treatment of hyperpiesis dependent upon primary contracted kidney you will not expect me to enter, otherwise than incidentally, for in it the hyperpiesis is but an incidental coefficient, while in hyperpiesia on the contrary it would seem that it is the high systolic and diastolic pressures themselves that do the mischief, or most of it. We do not know that the hypothetical pressor substance, if such be the cause, is otherwise poisonous; so long then as these pressures can persist without doing obvious damage, and this, unless perchance the patient be examined for some incidental reason, may be for many years,

medicine or medical advice is never thought of. Thus unhappily, but almost invariably, it is for deferred or ultimate effects that the patient seeks his doctor, who probably finds himself then face to face with an enlargement of the heart of long standing, perhaps of ten years or more, and a circulation strained beyond recovery. I think the longest period during which I have been able to watch over a case of hyperpiesia, as such, is eighteen years.

But too often our pupils are forbidden to treat the high pressures when discovered. They are told that this would be "to treat a symptom only, not the disease". But, until we find the key to the metabolic lock, why not treat a symptom, if the symptom itself be a nuisance? "Well," they say, "because it is unscientific"; besides, the high pressure is "compensatory"—another of our catchwords. Compensatory of what? Of a fall of pressure in the periphery beyond? But the "symptom" is the cause of this fall. Or it is to "eliminate a toxin"—another catchword!—How? by squeezing it out? If an ergot-like poison were crimping up one's arteriolar system, or directly irritating the vasomotor centre, would one decline to relax the system for fear of "destroying compensation"? Certainly not. The good reason why we do not prescribe vaso-dilators in these cases is because their effect is fugitive; they give no abiding profit, only a momentary assistance, thankful as we may be for the small mercy, at a pinch; as for instance in an attack of angina. Besides, the nitrites are useful aids otherwise also; as again in relieving some of the vaguer symptoms, especially headache and

oppression at the vertex ; or, a nitrite of amyl, for the arrest of a hæmorrhage (p. 67).

During *an acuter phase* of hyperpiesia, or of heart fatigue, or after a time of fag, a rest of ten days in *bed* is very helpful ; though on the other hand too much bed is unwholesome. Dr. Batty Shaw suggests that a patient with a proclivity to high pressures, if engaged in business, should take an occasional week-end in bed ; in bed, as we have seen, pressures may fall 20 to 40 mm. Hg. In graver cases, after a few such restful days massage may begin ; at first with short sittings, then watchfully increased. After a fortnight of this introduction the patient may be able to take regulated exercise according to his symptoms and powers. And thus we hope to see the tired, puffy, depressed, fretful, and flatulent man regain tranquillity and hope, and begin again to enjoy some of the duties and amusements of life. The more exacting methods of therapeutics can be arranged for periods of vacation, or of emergency.

Of course every possible source of local sepsis—ears, teeth, and so forth—will be thoroughly scrutinised, and any suspicious conditions corrected.

The diet of hyperpietics is not so simple a matter as has been supposed. Let us consider first the non-renal kind. We have been wont to attribute plethora, fulness of blood, "high tension", and so forth to overfeeding, especially on protein foods. We recall Clarendon's story of the third Earl of Pembroke, who " died of an apoplexy after a full and cheerful supper ". So, to lighten the burden, we cut down generous living, and especially meat, whether red or white. Thus we

find in practice that all hyperpietics have been " put on stoppages ". Nevertheless this privative system has disappointed us. Authors differ herein, no doubt; but it seems pretty certain that by moderation of appetite in all foods, by some restriction of proteins, of which we all eat more than we need, and by other wholesome rules and abstinences, we do gain some advantage, and a better foundation for more specific means; but if we expect by however skimpy and meticulous a dietary to control the blood pressures we shall be disappointed. Sometimes, it is true, a measure of success is thus obtained, but probably only in cases of heavy feeders and obese persons (p. 19) whose hyperpiesia is not deeply rooted, or is aggravated by " biliousness ".

Strouse and Kelman [1] set a watch on ten selected cases of pure hyperpiesia (kidney values normal), and found no parallel between the quantities of protein food (up to 150 gms. protein daily) and the arterial pressures; nor was there any parallel variation in the blood nitrogen, nor again in the renal excretion. Even strong animal soups had no such consequences. We shall not then cut diets down so far as to lower the patient's general condition, but prescribe a diet well balanced and moderate in quantities. Milk diet, which I have tried repeatedly, may be useful for a short time when the patient is put at rest in bed, but is no

[1] Strouse and Kelman, *Trans. Assoc. Amer. Phys.*, 1922, xxxvii. 22, and discussion. To infer the poisonous effects of excess of protein from the consequences of feeding raw meat to herbivora (*e.g.* rabbits) is absurd. They cannot utilise it, and die, simply of starvation. Even omnivora (rats, etc.) need fat also; cf. Arctic explorers and Esquimaux.

key to amendment. We remember that bed itself may account for a fall of 20-40 points. Metchnikoff's lactic treatment may or may not clear up intestinal putrefaction, but it has no effect upon arterial pressures. Dr. Bain,[1] it is true, found experimentally that on a chiefly vegetable diet the pressor base or bases normal to the urine fell off ; to rise again on the mere addition of milk. On a fuller diet he found no differences between butcher's meat, chicken, or fish. From the present point of view between the red and the white meats there is no difference. Three to five ounces of meat should, however, be the limit. Table salt does not itself raise arterial pressure, and in the non-renal cases, unless perhaps in case of cardiac anasarca, need not be restricted.

Of the importance of an artful reduction of obesity I have already spoken (p. 19).

Mosenthal,[2] in a discussion following Strouse and Kelman's paper, agreed that reduction of protein food does not itself bring down pressures, unless the reduction be so severe as to cause malnutrition and anæmia. In a patient under Dr. Bain's care, in the summer of 1924, treated by strict diet, the pressures did descend, it is true, from 200/180 to 134/80 ; on the other hand, in a patient aged 59, whom I saw in consultation about the same time, and who had been on a very strict diet for some months, the pressures still were 200/165, though the systolic had been 240. The heart was

[1] Bain, W., *Lancet*, 1911, i. 1409.

[2] Mosenthal, various papers (1917–22), *Med. Clin. North America*; *Amer. Journ. Med. Sci.*, Phila., 1920, clx. 808; and Nelson's *Loose-Leaf Living Medicine*, vol. iv. 503.

large, but the kidneys were doing well. His diet was porridge and milk for breakfast, a fish mid-day meal (meat rarely), and no formal dinner; in the evening a little bread and butter and milk was taken. No alcohol was, or had been, consumed.

Now if it be true that hyperpiesis depends upon some inwardly engendered poison constricting the muscular vessels—say upon some base or bases such as guanidine, iso-amylamine, or tyramine — these dietetic rules are mere groping; except in so far as they may bring some incidental benefit to any one who has fed himself too highly. But the flea is still in the blanket. If by diet we are to stop the generation, or compass the destruction, of some pressor poison it must be, as in the case of vitamines, by some far more intimate scrutiny than we have as yet made; and if the poison be the result of an eccentric proclivity, or default, or dislocation of some inward process, as of the liver, for instance, the patient, within hygienic limits, may eat what he pleases; unless an anti-fat regimen be required. A strictly peculiar diet is not only troublesome, but it tends to keep the patient's thoughts centred upon himself, which is bad for him. For this therapeutical reason it is unwise, unless of course during some period of special management or research, to register the arterial pressures too frequently, or at any time to repeat the readings to the patient. Assure him that you will keep him aware of the main bearings of his case; that records are to be taken as rarely as consistent with precaution, and that items will not be discussed. In this, as in all other respects, peace

of mind is to be promoted; business responsibilities and personal cares are therefore to be reduced, so far as may be without undue isolation, and bodily exercise, though by no means forbidden, kept within limits. All severe or sudden efforts should be avoided. The most important injunction is to lighten the evening meal (dinner or supper) according to the degree of the patient's illness; in the severer cases to make it almost a nominal refection.

These remarks on diet refer, as I have said, to the non-renal hyperpietics; on the larger question of the treatment of chronic renal disease I cannot enter. But I may say that in some of Strouse's renal cases, in which all protein had been cut out of the diet, though the blood nitrogen was diminished, there were no falls in arterial pressure. In cases of hyperpiesis, as in some other maladies, such as gout, we have a difficult course to steer between restriction of protein foods and consequent increase of fattening and flatulent carbohydrates. And in arterial cases we must recollect that the lungs of many elderly persons, if not emphysematous, are less active and depend more upon diaphragmatic than thoracic expansion. For such persons we must avoid bulky, windy foods—such as nursery puddings—which, by thrusting up the diaphragm, may hamper the breathing and distress a halting heart.

It is said that by the free use of acid fruits calcification of the arteries may be arrested, and even reduced; that in the femoral or popliteal artery, for instance, over some length of time, this reduction may be demonstrated by means of radiographic

pictures ; and that by this means the permeability of the vessels may be so far restored as to mitigate or remove functional failure of the parts supplied. But if this be true we should have still to inquire how far the calcification fortifies a perishing vessel.

Saline laxatives seem appropriate, especially on suspicion of a foul intestine ; in moderation no doubt they have their occasional value, but their regular morning use, in respect of the reduction of blood pressures, brings no advantage. Some of my medical hyperpietic patients who have tried them very carefully and hopefully, have been disappointed. Unless pushed to an extreme they bring no drop in mean blood pressure, and they are rather "lowering" if long continued.

A purely empirical but none the less efficient remedy in (non-renal) hyperpiesia is *calomel*, administered in fractional doses from time to time—say a quarter of a grain thrice daily for four or five days ; the course to be repeated every three or four weeks. The usual care of the mouth meanwhile will not be forgotten. The drug may act by quickening the portal factory, or possibly as an intestinal antiseptic. Kylin,[1] in hyperpiesia, administers calcium salts and atropine, given by the mouth, to moderate a supposed vagus predominance over the sympathetic system. And it is said that in hyperpiesia the calcium of the blood is diminished. At any rate the method is easy to try, and ought to be tried. In gout, I think, the blood calcium is supposed to be in excess.[2]

[1] Kylin, E., *Klin. Wchnschr.*, 1924, iii. 1712.
[2] Coates and Raiment, *Bioch. Journ.*, 1921, xviii. 5.

If in a case of hyperpiesia I were to suspect "intestinal toxins" as a cause I should give large doses of charcoal; and in such a case kaolin would be worth a trial. While such "symptomatic remedies" are being tried means will be taken of course to alter the conditions of toxic degrees of putrefaction.

Venesection is disappointing; its effect is transient. Some of my strong-minded patients have given the method a good trial; but the relief is not persistent enough to compensate the patient for the nuisance of it. Moreover, if continued long—say for six or eight bleedings at three or six months' intervals—the patient becomes languid and anæmic. It may reduce pressures temporarily, even from 220/160 to 145/95; but a less severe reduction is advisable: a considerable fall might favour thrombosis, in the auricles or otherwise. At a crisis venesection is valuable, for the nonce; but it is not for systematic repetitions. The one crisis for which it is indispensable is pulmonary œdema; then it must be prompt and combined with an injection of atropine; it may be useful also in overburdened heart, or, if foreseen, in threatenings of cerebral hæmorrhage.

The *vaso-dilators* are useful incidentally, especially in anginous states; but even erythrol tetranitrate, which is said to be the most abiding in its effects, makes no substantial impression on the march of the disease, whether renal or simple. These drugs are more needed in renal hyperpiesis, to relieve the more troublesome symptoms such as violent headache, or paroxysmal dyspnea. At times of crisis the late Sir W. Osler and others have pressed up the nitrites

to huge doses, in persons upon whom these drugs had been well tested. Sir William said he had never seen harm come of large doses if cautiously approached. I think he used to speak of 20-30 grains of sodium nitrite per diem! I may have administered half as much in a day. It is important to be sure of the quality of sodium nitrite.

The *hippurates*, recommended as moderators of arterial pressures by Dr. G. Oliver, one of our pioneers in medical piesometry, did not fulfil his expectations. The same is said to be the case of the benzoates; I understand that benzyl benzoate also has its advocates, but I cannot say much for it.

Iodide I usually administer in atherosclerosis, with or without high pressures, in grain doses twice or thrice daily; perhaps out of mere superstition? It may act indirectly through the thyroid, in which case the doses should be small and rare; or it may reduce the viscosity of the blood, or dilute its precipitates; or be of no use at all. I suspect its repute has grown out of its virtue in syphilis, with which in this lecture we are not concerned. It is said that cinnamon oil dilates the peripheral vessels (♏ x. dissolved in ♏ xx. of absolute alcohol and diluted with water); I know nothing of its virtues, but it is no disagreeable remedy at worst.

Few patients are in a position to select their own *climate*, but for those who may be so fortunate a warm equable climate offers a favourable change; there is less call upon the circulation for internal combustion.

Spa treatment is very helpful; but the particular Spa must be one where there is a physician diligent

in these cases. It is of no use to pay a single visit to a Spa physician, put down a couple of guineas, and take away no more than a blue paper ordering such and such baths and potations to be carried out by the bathmen, and a diet which the hotels ignore. Unless the kidneys are known to be working well, even water may be swallowed to excess. The patient should be under medical supervision almost day by day—at times indeed oftener; his blood pressures, his output of urine and its values recorded, his massage or exercises or diathermy controlled, and his diet regulated. The fresh air, change of scene, release from worries, and comradeship in a large campaign of cure, are far more important than the water chemicals.

The virtue of certain baths—saline or effervescent—in equalising pressures and promoting the normal streams of blood in the vessels has been proclaimed by certain physicians, sometimes in a manner which has hardly inspired confidence in the critical hearer. Experts in the method have not hesitated to submit to such baths hyperpietic patients suffering from degrees of substernal oppression amounting even to angina pectoris. In principle the method is by no means irrational; but personally I can say no more. It is evident that to avoid mischance it should be practised only by physicians proficient in the use of so potent an agency. A warm bath—say at 40° C., if taken without exertion, sends up the pressure by a few degrees; and so does a cold bath—say at 15° C.—but to no considerable height. Still, a vasomotor constriction intensifying pressure by a few

degrees only might do immediate harm. Such treatment should be very cautiously approached.

Antiseptics for the intestines, to counteract supposed meat poisons, if given by the mouth are by general agreement of little service; but in simple hyperpiesia Dr. Bain speaks well of washing out the colon with an alkaline sulphur water; in the renal cases he found no benefit from it.[1] From Metchnikoff's lactic method we gain nothing (p. 84); indeed, Dr. Ledingham has demonstrated its fallacies.

Diathermy—" d'Arsonvalisation " (by the " auto-condensation method ") is, I believe, the most valuable immediate aid we possess for hyperpiesia. It is said that radium emanations have the same virtue. It is true that diathermy does not—so far as we know—counteract the direct cause or causes of the malady; but until we know the primary causes we may be thankful to counteract the secondary. To restore order, we can only hit at what heads in the rebel crowd we see, whether of ringleaders or not; crude doctoring no doubt, yet often efficacious. However, diathermy needs cautious watching and adapting, and few radiologists can or will devote to

[1] In the *Lancet* of Aug. 23, 1924, Dr. Istvan (in Rusznyak's clinic) combated hyperpiesis (whether renal or not was not stated) with sulphur solutions given by intramuscular injection. One c.cm. of solution, containing 0·0001 gm. sulphur, is injected into the gluteal region, followed by a second in two or three days, and so forward at longer intervals; but the doses are increased gradually to 5 or even 10 c.cm. The injections are painful and generally cause some pyrexia, which is said to be beneficial. Four or five injections, however, are usually sufficient. By relaxation of angiospasm the blood pressure is considerably reduced and so remains, and symptoms are mitigated, or even abolished.

it the time and pains that it requires. Pictorial records are more attractive. So the results are too often disappointing. The late Dr. Roberts of Harrogate devoted himself to the work, and before the War he and I obtained many very satisfactory reliefs and cures. Dr. Hobson and Dr. Bain tell me the method is still in full use at Harrogate, and is rendering great and permanent service. In hyperpiesia it is given for about ten minutes daily, on the couch. A few casual, half-hearted, half-skilled, or more than half-sceptical applications are worthless. My friend Dr. William Brook of Lincoln in general practice has treated cases of hyperpiesia by diathermy for a few years, and speaks well of it. Of a certain patient whom lately I saw with him he reports that under twenty-minute sittings the pressures were gradually reduced from 220/110 to 170/90; indeed in cases of some inveteracy it is not wise to urge pressures hastily down below 160/80, if so far. Our patient after the course left home for a while; on his return the pressures were 200/100; so diathermy was repeated from April 4, 1924, and onwards; by April 15 pressures had fallen to 155/90 and he "felt remarkably better". By the way, in another patient, æt. 46, for whom diathermy did little, Dr. Brook tells me, he turned therefore to *thyroid extract* (1 gr. bis die), when the pressures fell steadily from 210 systolic (and 130 diastolic) to 170. There are a few cases in which we find this extract to be successful, perhaps in some of the obese? (p. 19). If, as Sir James Barr says, it raises the systolic pressure, while lowering the diastolic, it may be a double-edged

weapon. Euan Waller[1] carefully tested thyroid extract in hyperpiesia, and found it of no service; yet now and then it succeeds; perhaps in fat subjects (see p. 19). Dr. Cumberbatch, after much experience, kindly gives me his opinion that "the value of diathermy in hyperpiesia is well established".[2] Dr. Halls Dally[3] and Dr. F. H. Humphris[4] are of the same opinion. It is far from true that hot baths do as well; their effect at best is inconstant and fleeting.[5] Fontana[6] tested diathermy in forty-seven patients of hyperpiesia (non-renal), and found it lowered the pressures regularly. He adds that it promotes renal activity; and that if the kidneys do not respond there is no good result. He concludes that the effect is by renal eliminations; but presumably the renal response is less a means than a sign of the better vascular balance. Dr. Brockbank[7] used the remedy systematically for a year in each of twelve cases. In all he obtained a more or less permanent relief of symptoms and fall of pressures. One patient, whose systolic pressure was at first 190, had the

[1] Waller, E., *The Prescriber*, 1917.

[2] Cumberbatch, E. P., *Diathermy* (Heinemann), and private letters. With Dr. C. A. Robinson (*Brit. Med. Journ.*, 1923, ii. 54) he published some remarkable notes on the bactericidal virtue of diathermy (on the gonococcus in pelvic organs).

[3] Dally, J. F. Halls, *High Blood Pressure and its Management*, 1923.

[4] Humphris, F. H., *Brit. Med. Journ.*, 1923, ii. 314.

[5] I fear Galen's doctrine in this respect must be taken with some qualifications: "mollem reddunt arteriam humidi cibi; frequentiores balneae, somni multi, mollior vita, et deliciae", *De Praesagitione ex Pulsibus*, lib. ii.

[6] Fontana, *Gazz. di osped.*, Milano, 1914, No. 50 (quoted *Arch. des mal. du cœur*, Dec. 1915).

[7] Brockbank, E. M., *Lancet*, 1923, ii. 880.

treatment for nine months, when the pressure stood about 150, and one sitting every two months is keeping it there. Dr. J. Cowan[1] reports the same of thirty-eight cases. Pressures fell in every case but one, and these were for the most part cases of long standing. We cannot catch early cases. Dr. Cowan found, as I have found, that each patient has his irreducible minimum; "if thrust down the pressures pop up again". The falls at a sitting varied between 5-70 mm. Age and sex seem to make no matter, but the older folk need larger doses. Under the treatment headache, vertigo, dyspnea, insomnia, anginal pains disappear. Some cases of definite angina pectoris are said to have found permanent benefit by this means; the stress upon a sore aorta may be more or less permanently mitigated. I have tried it in one case of angina only; some little relief was obtained but no substantial benefit.

There are better methods for this malady.

In cases of hyperpiesia, renal or other, the heart, overworked and often fatigued, ought to be in agony with angina; yet angina is no character of these cases. Angina arises only when the strain upon the atheromatous aorta penetrates to and stretches its outer investment with its rich sensory end-organs (see p. 69).

Extract of the *corpus luteum* may prove useful in the menopause cases; in one or two in which I tried it no improvement was apparent, but I administered it by the mouth only.[2] Professor Vincent is of opinion that this extract is of doubtful virtue.

[1] Cowan, J., *Lancet*, 1923, ii. 884.

[2] See Moorhead, T. G., *Med. Press and Circ.*, 1923, N.S., cxv. 316.

A watchful eye must be kept also upon the state of the heart, and as a cardiac signal, the daily voidance of urine registered. Now and then an x-ray picture may be useful. *Digitalis* is invaluable in fatigued high pressure hearts, and must be vigilantly put in and out of use in accordance with the various and unstable indications ; especially with the tales of the pulse and the urinary flow. Perhaps many of us are not quite bold enough with digitalis. Half drachm doses of the tincture and yet more may lift a patient out of the pit ; so it is said : yet vomiting, once started by a large dose of digitalis, may be very difficult to subdue. Personally I have erred on the side of caution. *Diuretin* is a subordinate drug often helpful in the cardiac syndrom, especially if a diuretic action be required. Caffeine is effectual, but apt to spoil sleep.

If in dilating heart dyspnea be distressing, free *oxygen* may be helpful ; it should be administered under a hood so that it may be breathed at a concentration of 30 or 40 per cent. In urgent attacks small doses of *morphine*—about $\frac{1}{8}$-$\frac{1}{6}$ of a grain given under the skin—are a precious solace. For the insomnia of these cases, not directly due to the dyspnea, on the whole chloral answers best, and seems to have no depressant effect on the heart. The bases of the lungs cannot be watched too anxiously for warning signs of acute pulmonary œdema, lest there be any delay in the injection of atropine, and (probably) in copious venesection (p. 88).

To two more remedies I ought to make some allusion, as they have had some vogue in France and

Germany. The first is sodium silicate, administered by intravenous injection. My memorandum is taken from an article by Professor Kuhn of Rostock.[1] Dr. Kuhn's article is not very convincing; much of it is speculative or indeed metaphorical. His advocacy is rather for the relief of angina pectoris than of arteriosclerosis; but there is a lack of precision about the cardio-arterial conditions, and wide claims are made for its efficacy in other maladies. As to high blood pressures, the gain in a reported case of a reduction from 250 mm. to 205 mm. does not seem very precious. Notwithstanding, the remedy is an open one; it is recommended by physicians of repute, and under vigilant precautions may safely be tried. The silicate is to be obtained in ampoules from L. Zugmeyer, pharmacist, of Basel. Of the second remedy—"Animosa"—I can say still less; it seems to be a proprietary drug, but is declared to consist of extracts of the veins of young animals and of red blood cells.

Attempts have been made for many years to effect certain changes in bodily function by more direct action upon the vasomotor system. This has been attempted by sundry kinds of impression on the vertebral column, as by Dr. Chapman's ice and hot water bags; and again by Dr. Albert Abrams' percussion methods. Sir James Barr speaks with confidence of the effects of the Abrams' reflexes on the heart in periods of fatigue. On such testimony the method should receive careful attention. I am sorry to say that I have made no trial of it.

[1] Kuhn, M., *München. med. Wchnschr.*, 1921, lxviii. 1652.

Concerning the **treatment of apietic** (" decrescent " or " senile ") **atherosclerosis** I have nothing specific to say. Of course every lurking-place of sepsis must be searched—tonsils, teeth, ears, and so on. Such causes are more to be suspected perhaps in this malady than in hyperpiesia. Otherwise, what more can be done than to promote the general well-being as far as possible ? Iodide of potassium is given, and in this custom I follow the crowd, though in a rather casual and parsimonious way ; for most persons the iodide is an unpleasant drug. In syphilitic cases of course it is essential. And we should be glad to get rid of any excess of cholesterol in the system did we but know how to do it. Mild preparations of iron are distinctly beneficial to these patients.

A winter climate, mild and equable, is more important for these patients than for the hyperpietics. In all things we shall remember that they are wanting in reserve balances of various organs.

In fear of cerebral thromboses and consequent atrophies in vascular areas this or that occupation or amusement may be forbidden ; but it is not wise to knock an elderly man's life and habits about in fear of remoter contingencies. Men with curly limb arteries often live long, and keep up a little fishing or golf, while in others, whose accessible arteries are less deformed, decay may be progressing in vessels such as the coronary and cerebral, out of sight and mind, but of more immediate value to life.

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THE END

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